3-4

MAR 10 1928

ARCHIVES OF DISEASE IN CHILDHOOD.

EDITED BY

HUGH THURSFIELD, D.M., F.R.C.P., and REGINALD MILLER, M.D., F.R.C.P.

WITH THE HELP OF

H. C. CAMERON, M.D., F.R.C.P.
H. A. T. FAIRBANK, D.S.O., M.S., F.R.C.S.
LEONARD FINDLAY, D.Sc., M.D.
A. DINGWALL FORDYCE, M.D., F.R.C.P., EDIN.
C. MAX PAGE, D.S.O., M.S., F.R.C.S.
LEONARD G. PARSONS, M.D., F.R.C.P.
G. F. STILL, M.D., F.R.C.P.
Sir DAWSON WILLIAMS, C.B.E., M.D., D.Sc.

EDITOR OF THE *British Medical Journal*.

Vol. 3. FEBRUARY, 1928. No. 13.

CONTENTS

PAGE

Non-Tuberculous Fibrosis of the Lung in Children. By C. D. S. Agassiz, M.D., M.R.C.P., D.P.H., and W. J. Gill, M.D. 1

A Study of the Distribution of Rheumatic Infection in Children in Birmingham. By A. P. Thomson, M.D., M.R.C.P. 20

A Review of 180 Children Suffering from Rheumatism, Chorea and Carditis. By Robert Marshall, M.D., F.R.C.P.I., D.P.H. 28

Hæmorrhagic Disease of the Newborn. By Ruby S. Beveridge, L.R.C.P., M.R.C.S. 39

A Study of Two Types of Vomiting Associated with Acetonuria. By O. C. M. Davis, M.D., D.Sc. 49

ISSUED BY THE BRITISH MEDICAL ASSOCIATION.
London: British Medical Association House, Tavistock Square, W.C.1.

Yearly Subscription (6 numbers), 25/- *Single Number*, 4/6

GENERAL ADVISORY BOARD

H. T. Ashby (Manchester).
A. D. Blackader (Montreal).
W. R. Bristow (London).
Alan Brown (Toronto).
E. Cautley (London).
Carey Coombs (Bristol).
Glen Davison (Newcastle-on-Tyne).
T. Y. Finlay (Edinburgh).
C. B. Fleming (Glasgow).
Prof. John Fraser (Edinburgh).
Sir Archibald Garrod, K.C.M.G. (Oxford).
J. F. Gaskell (Cambridge).
G. R. Girdlestone (Oxford).
H. Tyrrell Gray (London).
Robert Hutchison (London).
R. C. Jewesbury (London).
F. S. Langmead (London).
C. P. Lapage (Manchester).
W. L. Maccormac (Balham).
T. P. McMurray (Liverpool).
Charles McNeil (Edinburgh).
A. E. Naish (Sheffield).
L. G. Parsons (Birmingham).
D. H. Paterson (London).
W. J. Pearson (London).
F. J. Poynton (London).
T. G. Pugh (Carshalton).
F. C. Pybus (Newcastle-on-Tyne).
Sir Humphry Rolleston, Bt. (Cambridge).
J. D. Rolleston (London).
J. C. Spence (Newcastle-on-Tyne).
C. W. Vining (Leeds).

NOTICE TO SUBSCRIBERS.

Subscriptions are payable to the Financial Manager of the British Medical Association who has charge of all financial matters concerning the ARCHIVES OF DISEASE IN CHILDHOOD. Address: British Medical Association House, Tavistock Square, London, W.C. 1.

NOTICE TO CONTRIBUTORS.

All papers submitted for publication should be sent to Dr. Reginald Miller, 110, Harley Street, W. 1. All other editorial matters should be referred to Dr. Hugh Thursfield, 84, Wimpole Street, W. 1.

Papers sent for publication should be typewritten. Illustrations will usually be inserted in the text itself, and care should be taken that the text is marked to show the desired position of each illustration.

Charts and curves accompanying papers should be carefully drawn, on white paper. Any lettering on these drawings should be lightly inserted in pencil.

Contributors will receive one proof in page, but it is assumed that all but verbal corrections have been made in the original manuscript; an allowance at the rate of ten shillings per sheet of sixteen pages is made for alterations in the proof (printer's errors excepted), and contributors will be responsible for any excess.

Contributors will be supplied with reprints of their articles at cost price if application is made when returning proofs. An estimate of costs will be given if desired on application to the Financial Manager of the British Medical Association.

Papers which have been published become the property of the ARCHIVES and permission to republish must be obtained from the Editors.

NON-TUBERCULOUS FIBROSIS OF THE LUNG IN CHILDREN.

BY

C. D. S. AGASSIZ, M.D., M.R.C.P., D.P.H.

AND

W. J. GILL, M.D.

From the High Wood Hospital for Children, Brentwood, Essex.

Since the work of Clark, Hadley and Chaplin was published on "Fibroid Disease of the Lungs" in 1894, a number of papers have been written on small collections of instances of this disease, or on individual cases, but so far no work appears to have been published giving the results of examination of a number of such cases by modern methods, e.g., X-rays, etc. We have been fortunate in having had under our supervision a considerable number of patients suffering from this disease and have investigated these patients by clinical, bacteriological and other methods, and by X-rays, and the results obtained seem worth recording, with a view to obtaining more general recognition of the occurrence of this disease.

Sex. The disease was found to occur equally in the two sexes. This accords with the experience of other writers.

Age. Fibrosis of the lungs may occur in children of any age. Not infrequently it occurs in children of under one year and we have records of cases, diagnosed on clinical evidence alone, under two years of age. Owing to the difficulty of obtaining blood in such cases we have not been able to investigate them as fully as the older children, but the evidence obtained from these older children is sufficient to warrant us in believing that the disease may be diagnosed in infancy.

Of our cases, the incidence was greatest in children from 5 to 10 years of age. Clark, Hadley and Chaplin showed that the incidence of the disease was greatest in patients under 15 years of age. The age incidence noted by these and other writers is rather above what we have stated, but this discrepancy appears to be due to the fact that these writers have included among their records a number of cases of bronchiectasis, which we regard as being more in the nature of a sequela of the disease.

Family History. Examination of the family history shows a marked contrast with that usually obtained in cases of pulmonary tuberculosis in children, where a large percentage show a history of contact with a case of tuberculosis. In fibrosis such a history is exceedingly uncommon. Of 37 cases examined, in only two was there definite history of a member of the family suffering from pulmonary tuberculosis. There appears to be no special familial tendency to fibrosis and in our cases no other members of the family were affected.

Previous History. Examination of the previous history shows a high incidence of measles, whooping cough or pneumonia. The other exanthemata only occurred in a few cases, e.g., scarlet fever (4), diphtheria (2), rubella (1), chicken pox (3), mumps (1), influenza (1), and in one case there was a history of empyema. Presumably the occurrence of these diseases had little bearing on the origin of the fibrosis.

But the number of cases in which there was a history of measles (24) whooping cough (19), and pneumonia (22), is large. The incidence of measles and whooping cough is not above that normally occurring among children, but the incidence of pneumonia is greater. The histories obtained showed that pneumonia occurred either alone or as a sequela of measles or whooping cough. In a further 6 cases there was a history of bronchitis and this figure does not include those cases in which a history of winter cough was given.

The striking fact brought out by this analysis is the high incidence of pneumonia—approximately 60% of the cases reported.

Symptoms and Physical Signs.

Cough is the most frequent symptom found. It has been described by some writers as being spasmodic in character and occurring in the morning when the child wakes, but in our experience it is more frequently present in the day time and is rarely spasmodic. The cough varies from time to time. It may be occasional, slight, or absent altogether at intervals ; but if absent it recurs at the onset of any slight catarrh of the lungs, and as these children are subject to catarrhal attacks, particularly in winter, the cough becomes evident or aggravated during the winter months. This aggravation of cough, or alternation of cough with periods of freedom from cough, may persist for long periods. Exertion, even slight, may be provocative of an attack of coughing usually of an irritative type. During the acute exacerbations to which these children are subject the cough becomes frequent and troublesome, but expectoration, if present, is scanty. Clark, Hadley and Chaplin describe vomiting as occurring as a result of a severe paroxysm of coughing, but the description they give appears to refer rather to that of a case of bronchiectasis than of fibrosis, and we have not observed such vomiting except in cases in which bronchiectasis has supervened on a pre-existing fibrosis.

Expectoration is conspicuous by its absence in the majority of patients. This is true of the disease in all stages, except the most extensive, and even then the expectoration is rarely large in amount. In our series the greatest quantity of sputum coughed up in 24 hours by any one patient did not exceed one ounce. The sputum consists of thick, sticky, gelatinous mucus, with possibly some muco-purulent material flaked through it.

As the disease progresses, the muco-purulent character of the sputum becomes more evident. In those cases which go on to bronchiectasis expectoration increases and develops the stale, sickly or fœtid odour characteristic of that disease. The glairy mucus obtained in cases of fibrosis is not offensive, nor fœtid, neither is it nummular. The difficulty of obtaining sputum from children is well-known, and it might be supposed that the explanation of the

absence of sputum was due to the children's swallowing it. We do not believe that this is a sufficient explanation, however, because children of similar ages, suffering from pulmonary tuberculosis can be taught to, and do, expectorate a quantity of sputum daily. More probably the quantity of secretion is so small as to be almost negligible, and the little there is is so tenacious and sticky that it is only coughed up with difficulty.

The sputum does not contain tubercle bacilli. Recent work has shown the importance of examination of the fæces for tubercle bacilli where no sputum can be obtained. Tubercle bacilli are not found in the fæces of children suffering from this disease.

Dyspnœa. Children whose disease is slight may not suffer from dyspnœa. In 40 per cent of our cases there was no complaint or evidence of dyspnœa. In the more advanced stages of the disease dyspnœa on exertion becomes very evident. Slight exertion, such as running up and down a flight of stairs, will produce dyspnœa out of all proportion to the amount of exertion undertaken. In the still more advanced cases dyspnœa may be present to some extent even when the child is at rest, but it is curious to notice that such dyspnœa, though quite evident to the observer, is apparently unnoticed by the child himself. If such a child be asked if he is out of breath he will almost invariably say "No," even though his breathlessness is sufficient to make speaking an obvious effort. That such children do not feel breathless is evident on watching them playing games such as football or netball. They take an active part in such games and do not appear to restrict their exertions in any way, though to the observer they appear markedly breathless. They differ in this way from children suffering from active pulmonary tuberculosis, who will avoid exertion which makes them breathless or tired.

Hæmoptysis rarely occurs. Slight staining or streaking of the sputum with blood takes place occasionally, but a larger hæmoptysis is of rare occurrence, and if it occurs there seems no tendency for it to recur. Consideration of the pathology of the disease would lead one to expect this, as in fibrosis of the lung there is not that erosion and breaking down of tissues that occurs in pulmonary tuberculosis, and such bleeding as does occur is probably due to rupture of a small vessel in the bronchial mucous membrane.

Pain is seldom present and is never severe. When present it is located in one or other side of the chest, and partakes rather of the sensation of a pulling or tugging on the affected side.

Cyanosis is one of the most constant signs of this disease and in our opinion one to which insufficient attention has been paid by previous writers. In children with extensive fibrosis the lips, cheeks, and tips of the ears are bluish or purple in colour, the surrounding skin being dusky or dark sallow. In less extensive disease only the lips and cheeks may show a cyanotic tinge, and in still less extensive disease the lips alone may be affected. The intensity of the cyanosis is increased by exercise or cold weather. Children with marked cyanosis as a result of fibrosis of the lungs tend to develop a coarseness of the features which may be such as to suggest the development of slight clubbing, particularly of the tip of the nose.

One further point regarding cyanosis may be noted here. We have observed that when children, who are suffering from extensive fibrosis of the lungs and are cyanosed, develop tuberculosis, the cyanosis diminishes in degree as the tuberculosis develops. The explanation of this change appears to be found in the pathological changes taking place in the diseased tissue to which we refer more fully below.

Clubbing of the finger tips was found in two-thirds of the cases and varies in degree according to the severity of the disease. In cases of slight disease there may be only slight curving of the finger nails. Cyanosis and clubbing appear to be related. In 75 per cent. of our cases the two signs were present

FIG. 1. N.G. Shows apparent bulging of right lung to left side and displacement of heart.

and it was observed that, though cyanosis without clubbing did occur, rarely, if ever, did clubbing occur without cyanosis. The clubbing is more marked than that found in children suffering from pulmonary tuberculosis. Indeed, in our experience, clubbing is not a marked feature of pulmonary tuberculosis in children, except where tuberculosis has been superimposed upon a pre-existing fibrosis of the lungs. In such cases the clubbing tends to diminish with the extension of the tuberculous process.

Appearance and Physique. Children, whose disease is of short duration or slight, may be up to or above the average size for their age ; they may be plump and healthy-looking, a striking feature being the high colour of their cheeks.

In cases of longer duration the cyanosis is more evident, the coarseness of the features already described may be present, and such children are under the average in weight and height for their age. The extremities, particularly the hands, may be bluish even in warm weather. In cold weather the cyanosis of the features and extremities becomes more marked and gives the appearance of the child being "blue with cold," but such children do not complain of feeling cold nor do they appear to suffer from the cold more than other children. In cases of long standing the physique is poor. Evidence of rickets may be present, particularly in the chest.

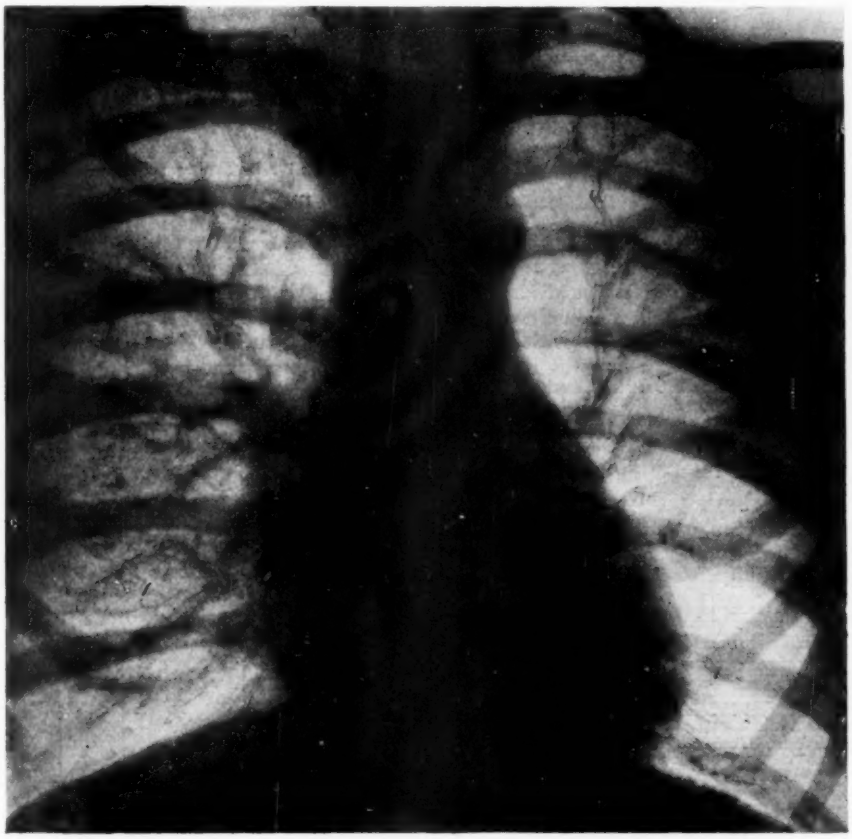


FIG. 2. L.M. Shows increase of root shadows radiating to base and to less extent to upper part of lungs.

Physical Examination of Chest. On deep inspiration there is either general diminution of the expansion of the chest or diminished expansion of one side, and indrawing of the lower intercostal spaces (8th to 10th) may occasionally be seen over the affected side. Displacement of the cardiac impulse is evident where such exists. On palpation there may be no alteration of vocal fremitus, but more usually it is diminished, though never absent altogether. On percussion the note over the affected lung is impaired even in the early stages of the disease, this impairment being most evident at the base of the lung.

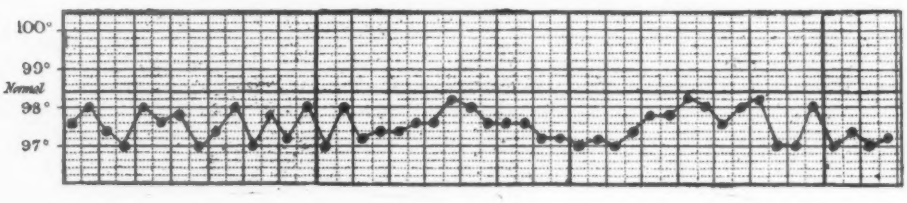
Where the note is impaired over the whole lung, the dullness increases in degree from apex to base, and in this contrasts with that found in cases of pulmonary tuberculosis in children, in which the dullness is most evident at the apex of the lung and diminishes towards the base. Though one lung usually gives evidence of being more affected than the other, the disease is probably always bilateral, and in many cases impairment of note over the whole of one lung is accompanied by impairment at the base of the other lung. The dullness is never so absolute as that found over fluid.

On auscultation there may be no adventitious sounds present, though the breath sounds may be diminished. More usually are found râles of a coarse, dry, possibly leathery character, more evident or more profuse towards the base. Not infrequently crepitations may be heard at the base, giving the impression that they are being produced near the surface of the lung. We regard this type as indicating greater involvement of the pleura. Bronchial breathing may be present opposite the inferior angle of the scapula, and may extend along the vertebral border and be of such intensity as to suggest the presence of a cavity. The extent, frequency, and profuseness of the adventitious sounds vary from time to time. At one examination the whole chest may be filled with loud consonating râles and at the next examination a few days later there may be complete absence of adventitious sounds. So frequently does this occur that we regard it as being characteristic of the disease.

During the pyrexial attacks (described below) very little evidence of bronchopneumonia may be found by auscultation, though X-ray examination shows some consolidation, but there may be an increase of the signs which are present when the child is apyrexial. The râles give the impression of being moister in character or more profuse in extent, but, owing to the presence of moist sounds in the chest when the child is apparently well, it is often extremely difficult to say whether there is any increase in their extent or not. Such cases seen for the first time during a pyrexial attack are sent to hospital as pneumonia. If these attacks recur, the history given is one of recurring attacks of pneumonia; that the chest does not clear between the attacks is overlooked, and thus the true nature of the child's illness is not recognised. Such a pneumonic attack may cause death in a few hours or days.

Temperature. This is usually normal, but certain variations from the normal occur, and are described below. Though there may be no rise above normal, we have noticed that an irregularity within normal limits occurs in the form of a curve over a period of two or three weeks (Chart I).

Chart I.



The other variations from the normal are as follows :—

The temperature, which has previously been normal, may suddenly rise sharply to 100° or 101° F. or higher, and after 24 or 48 hours fall sharply (Charts II and III.) During this period the child appears comparatively well, does not complain of feeling ill, the pulse rate is raised, but the respiratory rate is unchanged, and the child rarely requires to remain in bed for more than a day or two. If an X-ray photograph is taken during this period, evidence of inflammation is found round the bronchi, or a patchy consolidation, usually at the base or near the root of one lung.

CHART II.

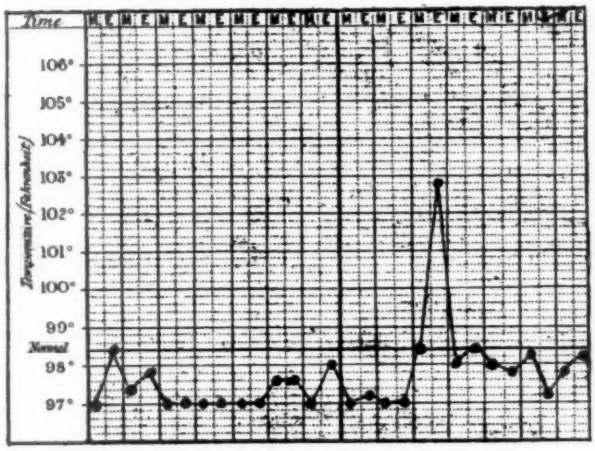
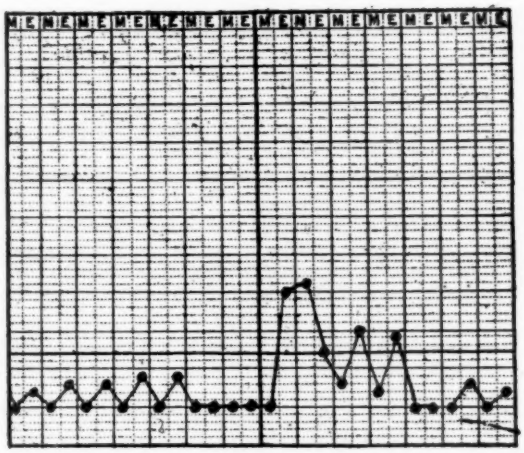
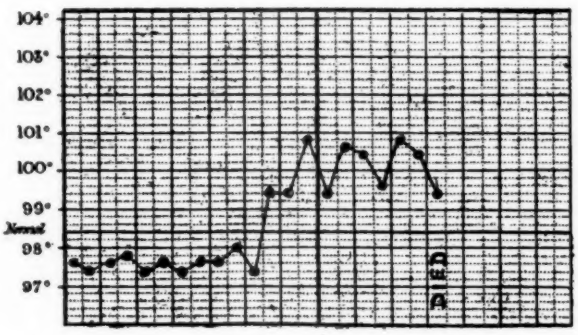


CHART III.



The second variation that may occur is observed as a rule in patients with extensive disease. In this type the temperature rises sharply to 102° F. or higher and remains raised for some days, usually a week or so, and resembles the temperature curve of lobar pneumonia (Chart IV). During this attack the child looks anxious, the pulse is rapid, the cyanosis becomes extreme, the breathing laboured and wheezy, and the respiratory rate is increased, though not to the same extent as in lobar pneumonia.

CHART IV



Weight. Only 25 per cent. of our cases were up to, or above, the average weight for their age, and one-third of the cases were 14 lbs. or more under weight. This under-development did not appear to be due to the extent of the damage to the lung, for the diminution in weight was as marked in the cases in whom the blood-oxygen content was nearly normal, as in those in whom it was markedly diminished.

FIG. 3. R.A. Shows massive root shadows extending particularly to bases.

Examination of the previous history showed that under-development in weight was most marked where the disease was of long duration, though not necessarily extensive. The repeated attacks of catarrh necessitating confinement to the house or bed with loss of appetite and general malaise may help to explain the lack of development. It is possible that bad home conditions or under-feeding may contribute, but we do not believe that these factors fully explain it, for children, who have been under treatment in hospitals or institutions for years, and thus have been living in stable and satisfactory surroundings, may show as marked under-development of weight as children who have been living at home.

Von Pirquet Reaction. In the majority of cases the von Pirquet reaction is negative. In our series of cases 87 per cent. gave a negative result and 13 per cent. (5 in 37) a positive reaction. The high percentage of negative results obtained is striking and lends support to the view that these cases are not tubercular in origin.

FIG. 4. C.B. Shows honeycomb appearance.

Wassermann Reaction. The possibility of fibrosis being due to syphilis led us to have the blood tested in all cases. In the majority the results were negative, but 8 per cent. (3 in 37) gave a positive result. The patients with a positive reaction did not appear to differ in any way, either in history, physical signs, symptoms, or radiologically, from those in whom the test was negative. Anti-syphilitic treatment did not appear to have any effect on the disease. The percentage of positive results obtained, however, suggests that syphilis may be a contributory cause of the disease, and further investigation of this point is necessary.

Blood-Oxygen Content. Lundsgaard and Van Slyke have shown that cyanosis develops as the result of want of oxygenation of the blood, and that when the oxygen unsaturation rises above 6·7 volumes per cent. in the capillary blood, signs of cyanosis develop. The frequency with which cyanosis occurs in children suffering from this disease led us to investigate the blood-oxygen content in the hope that we might obtain additional information which would be of use in diagnosis.

Venous blood was taken for this purpose. The blood-oxygen content was found to be diminished in every case. It was usually most diminished where the cyanosis was most marked, but even in cases in which cyanosis was slight the blood-oxygen content was diminished as compared with the normal. In some cases a blood-oxygen content of 6·7 volumes per cent. was observed. The diminution of blood-oxygen appeared to depend on the extent of the fibrosis rather than on the length of history of the case.

As a control to these observations blood was taken from children in whom no disease could be detected, and in these the blood-oxygen content was found to be normal. In order to compare the above findings with those obtained in pulmonary tuberculosis, the blood of children suffering from slight but active pulmonary tuberculosis, in whom the diagnosis had been confirmed by finding tubercle bacilli in the sputum, was examined. In all these cases the blood-oxygen content was normal. In cases of pulmonary tuberculosis of long standing, which we believed to be examples of tuberculosis supervening on a pre-existing fibrosis, the blood-oxygen content was diminished.

TABLE :

TYPICAL BLOOD-OXYGEN CONTENTS IN DIFFERENT GROUPS.

	Disease.	Blood-oxygen content (vols. per cent.)
N.M. ..	Extensive fibrosis of both lungs ..	6·81
L.B. ..	Extensive fibrosis of both lungs ..	6·01
A.W. ..	Fibroid signs at both bases	11·88
E.F. ..	No evidence of disease	12·80
E.W. ..	Pulmonary tuberculosis	12·40
W.C. ..	Pulmonary tuberculosis (T.B. +)	13·40
J.C. ..	Pulmonary tuberculosis superimposed on fibrosis (T.B. +)	8·23
E.C. ..	Pulmonary tuberculosis superimposed on fibrosis (T.B. +)	9·21

At this stage it may be worth while considering shortly the pathological changes that take place in pulmonary tuberculosis and in fibrosis of the lung, in order to explain the different blood-oxygen contents in the two diseases.

In fibrosis of the lungs the fibrosis occurs around the bronchi, in the interlobular septa, and in the alveolar wall. As a result of the involvement of the alveolar wall the absorption of oxygen from the alveoli is interfered with, though the circulation of blood through the capillaries surrounding it is maintained. The result is that the blood returning to the heart from the area of the lung affected is un-aerated and thus is produced what Lundsgaard and Van Slyke term an "un-aerated shunt." The proportion of blood affected varies with the extent of lung involved, and when more than one-third of the blood is involved the drop in the oxygen content is sufficient to produce cyanosis.

In tuberculosis, on the other hand, though the tubercle may form in the alveolar wall and may interfere with the normal function of the alveoli to some extent, it does not produce an "un-aerated shunt" because the blood vessels in the tuberculous deposit become thrombosed and, circulation through them being thus prevented, the blood is diverted through other parts of the lung and is oxygenated.

We noted that when a cyanosed patient suffering from fibrosis develops tuberculosis, the cyanosis diminishes in degree with the increase of the tuberculous process. The explanation of this would appear to be that when tuberculosis develops in the area of fibrosis the blood vessels in the tuberculous deposits become thrombosed, and the blood supply is thus cut off from this area and diverted through the healthy parts of the lung. As the tuberculosis spreads through the fibrosed lung, the area of the shunt becomes reduced and the cyanosis diminished. If these arguments are correct, the examination of the blood-oxygen content should give the following results :—

1. In fibrosis the blood-oxygen content should be diminished.

2. In tuberculosis the blood-oxygen content should be normal (except in massive infection of the lung).

3. In fibrosis in which tuberculosis developed, the blood-oxygen content should increase with the increase of the tuberculosis.

4. In tuberculosis which was healing, i.e., fibrosing, the blood-oxygen content should decrease as healing advanced.

We have already dealt with the first two points. With regard to the third and fourth we have so far not had an opportunity of making a sufficient number of observations to be of value.

X-ray Examination. On screen examination the apices light up well and equally ; there is some increase of root shadows extending particularly towards the base ; and there may be irregularity of the outline of the diaphragm on deep inspiration, and blurring of the cardio-phrenic angles. There is no evidence of enlargement of the bronchial glands.

Radiograms may show some deflection of the trachea to one or other side. Occasionally there appears to be some bulging of the less affected lung towards the opposite side, suggesting the pushing over of the mediastinum, but whether this deflection is due to a pulling over as a result of the fibrosis of the lung, or to a pushing over from emphysema of the less affected lung, is not yet clear, but it seems probable that it is in the nature of a pulling over as a result of contraction of the lung. The heart shadow may be unaltered in position or may be displaced. The shadows at the root of the lung are increased in extent. In many cases these are dense and massive, extending from the

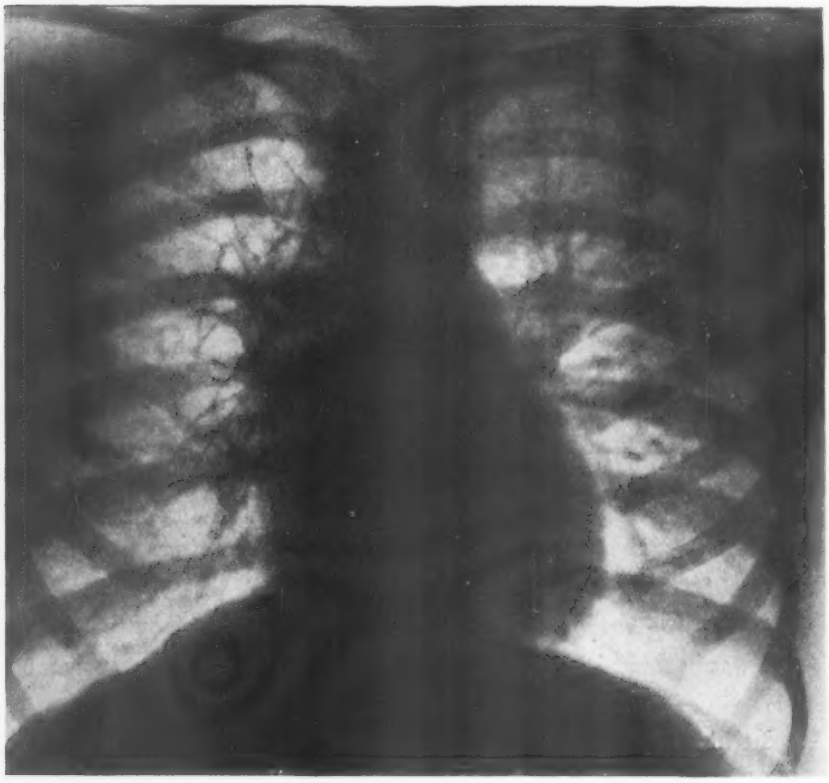


FIG. 5. C.L. Shows star-shaped shadows centred round a bronchus.

level of the third to the sixth or seventh rib anteriorly; and from the central shadow there radiate out into the surrounding lung heavy, streaky shadows most evident towards the base, though at times radiating shadows may be seen extending to the upper part of the lung. They are not usually marked in the middle portion of the lung. The normal reticular formation may be more evident than usual and in some cases a markedly honeycomb appearance, particularly of the upper part of the lung, may be present. Star-shaped shadows, centred round what appears to be a small bronchus seen in cross section, may sometimes be observed. The apices are clear.

Irregularity of the diaphragmatic outline is of frequent occurrence, and may be present when the root and basal shadows are not marked. The cause of this irregularity is an interesting point, and we believe that it may be explained as follows :—

The lung is most fixed at its root, the outer portions contracting and expanding with respiration. When fibrosis occurs it is found around the bronchi and in the alveoli and interlobular septa, and as a result of it there is a diminished expansibility of the portion of the lung affected. The diaphragm is retained in apposition with the base of the lung by the negative pressure in

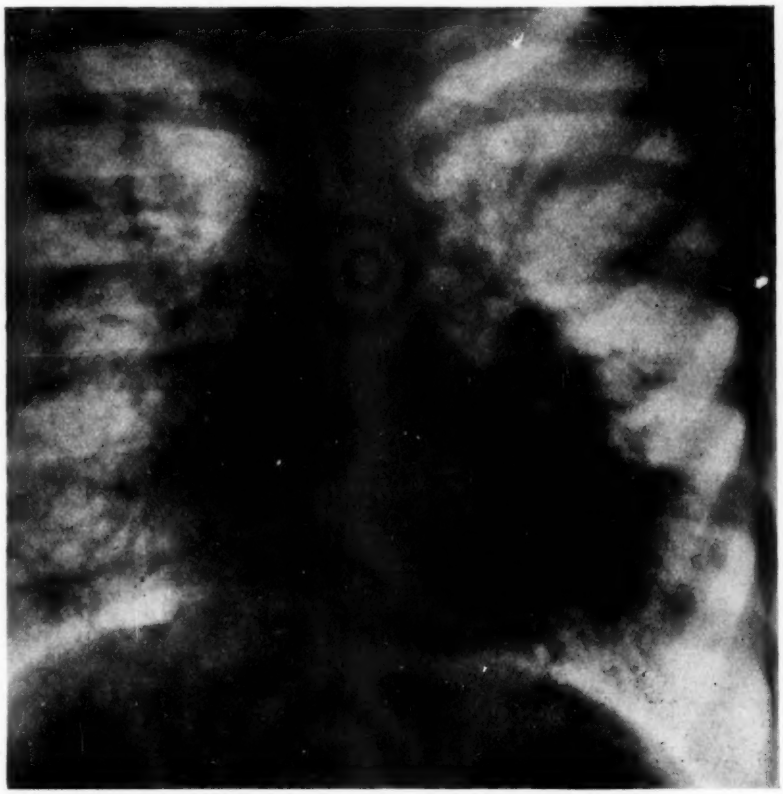


FIG. 6. R.A. Same case as Fig. 3, showing dark shadows which may be found during a pyrexial attack.

the pleural cavity. Now, if fibrosis occurs in the lung around the bronchi extending to the base, the elasticity of this portion of lung is reduced, and the root of the lung being the most fixed point, the area of lung, and consequently the diaphragm, at the lower part of the fibrosed area, will move less on inspiration than the surrounding lung tissue and in consequence irregularity will show in the diaphragm. These irregularities of the diaphragm are invariably present in its inner two-thirds as would be expected if the explanation given above is the correct one. It seems improbable that such irregularities are due to adhesions. If they were, one would not expect to find an irregularity

on deep inspiration, as the elasticity of the lung would not be affected, and further, there seems to be no reason why adhesions should be restricted to the inner part of the diaphragm.

Though the increased root and basal shadows may be more evident in one lung, there is usually some increase in the other lung. Radiograms taken during a pyrexial attack may show dark shadows near the root or base of the lung.

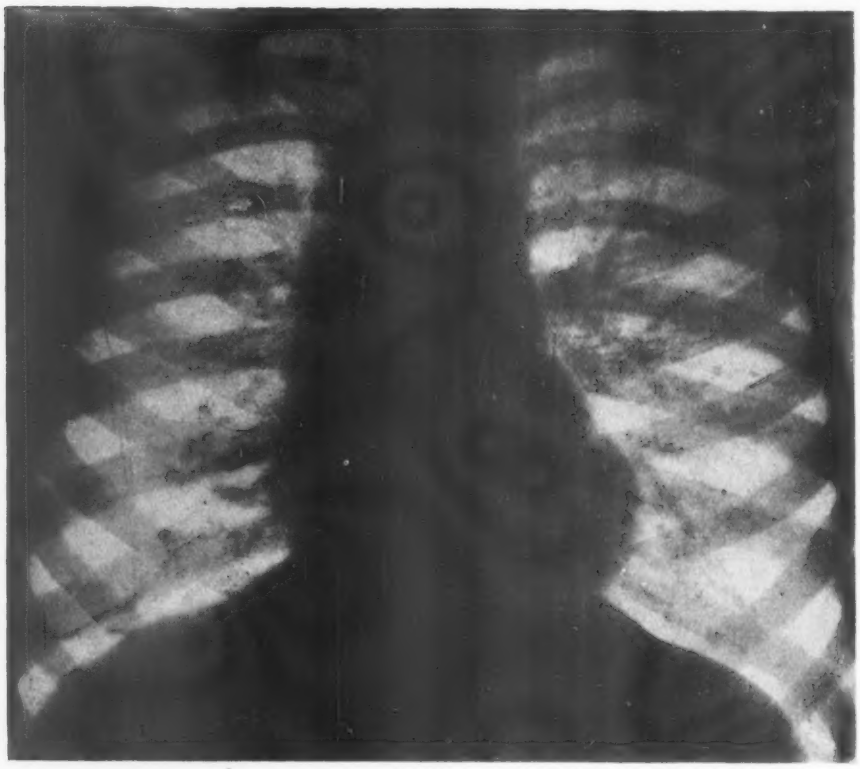


FIG. 7. J.R. Showing thickening round bronchi during a catarrhal attack.

COMPLICATIONS.

The subjects of fibrosis appear to be more liable to complications of a septic nature than other children. They frequently show evidence of antecedent rickets. Otorrhœa is not uncommon and such minor forms of infection as tonsillitis, impetigo, and catarrhal affections of the lung occur more often. The bronchopneumonic attacks to which these children are subject have already been described.

Clark, Hadley and Chaplin noted the occurrence of albuminuria in their cases but we have not been able to confirm this. Possibly the fact that they were referring to adults in whom the disease was of long standing, or in whom bronchiectasis was developing, may explain this.

Diagnosis.

The diseases from which fibrosis has to be distinguished are particularly :— (1) Tuberculosis ; (2) Chronic bronchitis ; (3) Pleural effusion ; (4) Thickened pleura ; and (5) Bronchopneumonia.

1. *Tuberculosis.* The importance of distinguishing between this disease and pulmonary tuberculosis is evident, but that it is not appreciated sufficiently is shown by the fact that the cases upon which this paper is founded were sent to hospital as cases of pulmonary tuberculosis. Consideration of the following factors is usually sufficient to distinguish the two diseases.

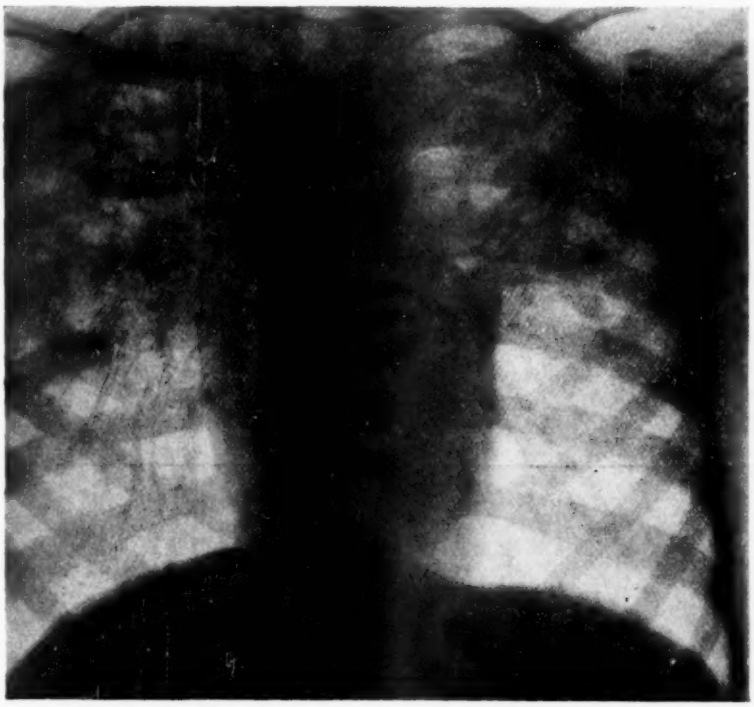
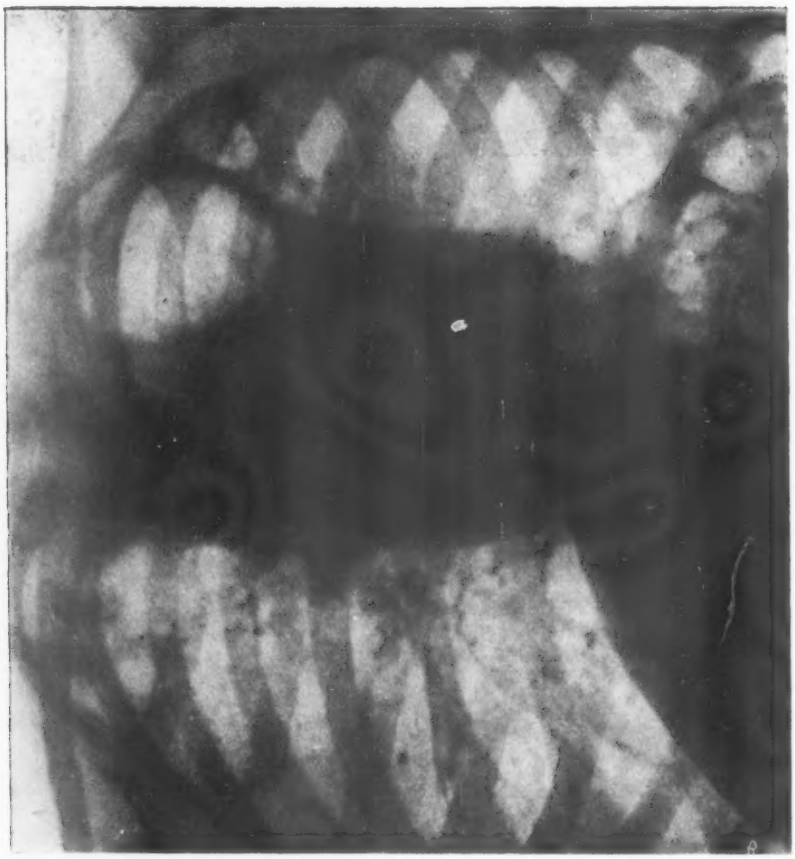


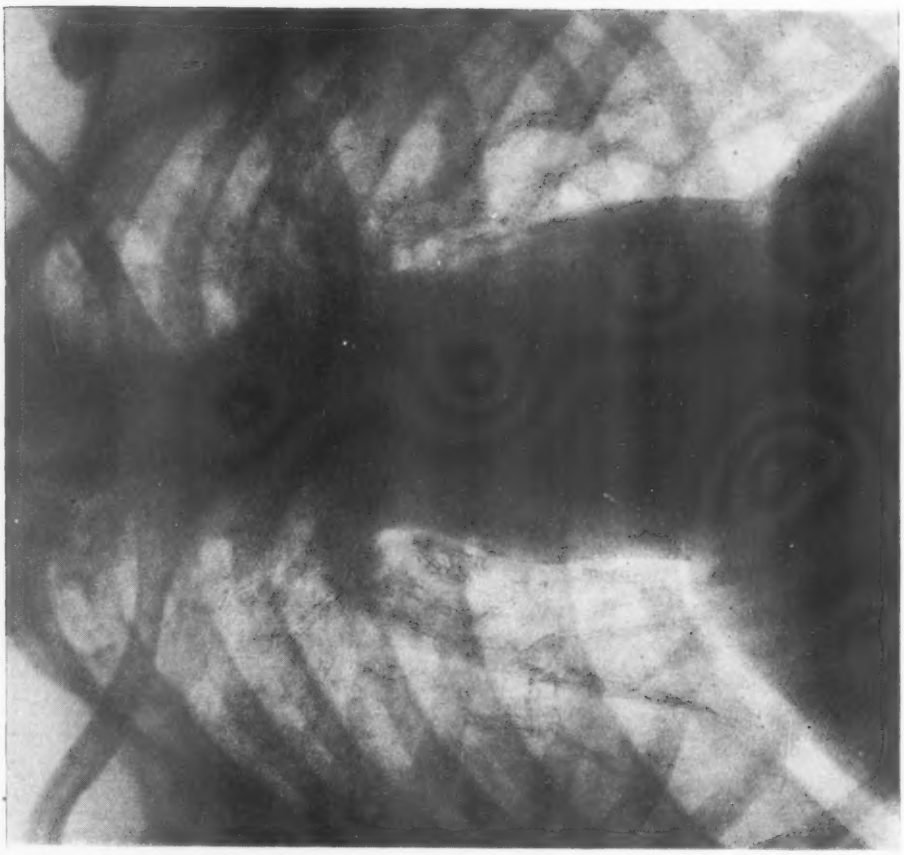
Fig. 8. I.B. Shows typical fibrosing pulmonary tuberculosis.

In the majority of cases of fibrosis there is a history of an attack of pneumonia, either unaccompanied, or as a sequela of measles or whooping cough. There may be a history of repeated attacks of pneumonia. In others the history is one of repeated attacks of bronchitis. In pulmonary tuberculosis there is frequently a history of contact with a case of pulmonary tuberculosis, but in fibrosis such a history is not common.

The characteristic aspect has been described, and is in contrast to that of children suffering from pulmonary tuberculosis.

Children suffering from pulmonary tuberculosis are commonly pale ; they are not under-developed unless their disease is of long standing or progressing, and, as they recover, they gain weight rapidly, and usually reach the average weight for their age in a comparatively short time. The symptoms, physical





FIGS. 9 & 10. Two cases of pulmonary tuberculosis to show contrast between this disease and fibrosis.

signs, X-ray examination, examination of sputum and fæces, Wassermann reaction, and blood-oxygen content all give evidence which must be considered in attempting to arrive at the correct diagnosis.

The X-ray photograph in pulmonary tuberculosis shows mottling or woolliness more marked at the apices. Cases in which the tuberculosis is healing or healed show, in addition to this woolly mottling, shadows of irregular density particularly near the apex.

The diagnosis from hilum tuberculosis is one which causes more difficulty, but there are a few points which seem to us to warrant the belief that what we have described is not hilum tuberculosis. Many of these cases begin in infancy. On examination of such a case are found numerous râles at both bases, but the X-ray photograph only shows an increase of root shadows. It is difficult to believe that an infant with extensive signs, but apparently in good health, and with little evidence of disease in the lungs as shown by X-ray photographs, is suffering from tuberculosis, which is admittedly a most fatal disease in infants. To older children the same argument applies though to a less extent. In these children it is characteristic to find extensive physical signs, but an X-ray picture which shows remarkably little change. In tuberculosis, on the other hand, the X-ray picture usually shows evidence of far more extensive disease than is given by physical signs. Further, in pulmonary tuberculosis the signs are more evident at the apex, whereas in fibrosis they are more evident at the base of the lung.

It may be argued that the picture we have described is one of so-called 'hilum tuberculosis' in which the disease has gradually become quiescent, and that as a result fibrosis has taken place in the peribronchial areas, producing the typical X-ray picture.

Such an explanation is at first sight plausible, but on reflection it cannot be maintained. In the first place it makes no attempt to explain the occurrence of cyanosis. Secondly, if healing of the tuberculosis is taking place in the peribronchial areas, the condition of the child should improve. The history of cases of fibrosis is, however, that of a slowly progressive disease. Again, the strongest argument against this theory is the existence of cyanosis with, in consequence, a lowered blood oxygen content. The presence of cyanosis in itself shows that at least one-third of the blood has not been oxygenated. Now, if the fibrosis is the result of a healing tuberculosis, the tuberculous deposits must have been in the alveolar wall as well as in the peribronchial tissue in order to produce interference with oxygenation, so that at least a large portion of the lung area must be affected by a fibrosing tuberculosis which, in contrast to cases of pulmonary tuberculosis, confirmed by finding tubercle bacilli in the sputum, shows no sign in a radiogram except in the peribronchial tissue. Such a proposition cannot be seriously maintained.

(2) *Chronic Bronchitis.* In distinguishing between chronic bronchitis and fibrosis of the lung the following points should be borne in mind. Chronic bronchitis tends to produce emphysema and evidence of this should be sought for. The percussion note is not permanently impaired, and there is no

displacement of organs. Contraction of the chest on the affected side, displacement of organs towards the affected side, impairment of percussion note, cyanosis and clubbing of the finger-tips should suffice to distinguish the two diseases.

(3) *Pleural Effusion.* The diagnosis between fibrosis of the lung and pleural effusion is not difficult. The distinguishing points are that in pleural effusion the dullness is more wooden, vocal fremitus may be absent, and displacement of the organs is away from the affected side. In contrast to this in fibrosis there is not a complete absence of vocal fremitus, and any displacement of organs is towards the affected side. The X-ray picture in the two diseases is distinctive. The use of the exploring needle would settle a doubtful case.

(4) *Thickened Pleura.* A diagnosis between fibrosis of the lung and thickening of the pleura is not one of much practical importance. In extensive fibrosis the pleura is probably always thickened, and in thickening of the pleura which follows on pleurisy or pleural effusion there may be a pleurogenous fibrosis. Apart from this the main point of difference is that in thickening of the pleura *per se* adventitious sounds are absent at all times. X-ray examination may show some diminished translucency on the affected side.

(5) *Bronchopneumonia.* In the acute stages it may be difficult to distinguish the diseases, but evidence of clubbing of the finger-tips or displacement of the heart will indicate the true cause of the bronchopneumonia. In cases of fibrosis the persistence of the physical signs when the child is convalescent serves to bring out the true character of the disease.

The diagnosis from such rare diseases as sarcoma of the lung, cysts, etc., is not of much practical importance owing to their rarity, but apart from the physical signs X-ray examination should be sufficient to eliminate the diagnosis of fibrosis in most cases.

Prognosis.

From a practical point of view it may be argued that a diagnosis of fibrosis of the lung is not of much importance, but as we believe that this disease is more common than is generally believed, and less frequently recognized than it should be, and as so many of these cases are labelled and treated as tuberculosis, from an economic point of view at least it merits attention.

The prognosis in these cases is vastly different from that of tuberculosis. Fibrosis of the lung is probably a slowly progressive disease, but the subjects of it may live many years and lead active and useful lives. They are subject to catarrhal attacks and may develop broncho-pneumonia which may cause death. A certain number appear to develop tuberculosis, but in such patients we find that the tuberculous process is of slow growth and, in contrast to children in whom pulmonary tuberculosis develops but is not superimposed on a pre-existing fibrosis, they may live for a number of years, e.g., six, eight or more. Other cases develop dilatation of the bronchi and become bronchiectatic. Possibly in some cases the signs may disappear but so far we have not been able to collect sufficient evidence to say whether this occurs or not. Owing to their susceptibility to septic infections the onset of such infections

may terminate these cases. In one case (not included in this series) infective endocarditis followed on fibrosis resulting from injury, and in this case we were able to confirm the diagnosis of both diseases at post-mortem.

One further point in connection with this disease is worthy of remark, as it does not appear to have been noted by other writers. We have frequently observed that the subjects of this disease take anæsthetics badly, even such anæsthetics as nitrous oxide, and it is within our knowledge that cases operated on for such diseases as appendicitis have collapsed and died shortly after the operation from no apparent cause. We consider that if attention were directed to this point valuable information might be obtained.

Treatment.

Very little need be said regarding treatment, as it is mainly palliative The ordinary open-air treatment in convalescent homes, or sanatoria for children, suits these children very well.

Prevention, so far as possible, of the onset of catarrh should be practised. With the onset of any fœtor of the breath, creosote in increasing doses should be given, and children of tender years will take up to half a drachm, thrice daily, without complaint. The possibility of treatment by vaccines suggests itself, but we have had no experience of their use.

BIBLIOGRAPHY.

Atkinson, D. W., *Amer. J. Med. Sc.*, Philad., 1925, CLXX, 693.
Bissell, F. S., *Amer. J. Roentgenol.*, N.Y., 1925, XIII, 126.
Carroll, W. F., Gibson, C. B., Banyai, J. A., *Amer. Rev. Tuberc.*, N.Y., 1925, II, 40.
Clark, A., Hadley, W. J., & Chaplin, A., *Fibroid Diseases of Lung*, Lond., 1894.
Davis, K. S., *Radiology*, Minn., 1924, III, 150.
Duhem, P., *Arch. de méd. enf.*, Paris, 1921, XXIV, 663.
Dumarest, F., *Ann. de méd.*, Paris, 1922, T., XI, 219.
Field, C. G., *Amer. J. Med. Sc.*, Philad., 1920, CLIX, 442.
Hebert, G. T., *Lancet*, Lond., 1922, i, 1145.
Jermain, M. L. F., *Tice's Practice of Medicine*, 1923, V, 534.
Kahn, M. and Sloan, M. F., *Radiology*, Minn., 1925, IV, 198.
Lyter, J. C., *Med. Clin. N. Amer.*, Philad., 1920, IV, 819.
Lungsgaard, C., and Van Slyke, D.D., *Medicine*, Balt., 1923, II, 1.
Mills, H. P., and Watkins, W. W., *Radiology*, Minn., 1925, IV, 178.
M'Neil, C., *Edin. Med. J.*, Edin., 1925, XXXII, 107.
M'Neil, C., *Trans. Med. Chir. Soc.*, Edin., 1924-25, XXXIX, 152.
Overend, W., *Tubercle*, Lond., 1920, I, 547.
Palasse, M., *Lyon Méd.*, Lyons, 1925, CXXXV, 46.
Palasse, M., and Badolle, *Ibid*, CXXXVI, 691.
Riviere, C., *St. Bart. Hosp. Rep.*, Lond., 1905, XLI, 123.
Sante, L. R., *Radiology*, Minn., 1924, III, 128.
Tallermann, K. H., *Arch. Pediat.*, N.Y., 1925, XLII, 176.
Young, F. H., *Charing Cross Hosp., Gaz.*, Lond., 1926, XXVI, 139.

A STUDY OF THE DISTRIBUTION OF RHEUMATIC INFECTION IN CHILDREN IN BIRMINGHAM.

BY

A. P. THOMSON, M.D., M.R.C.P.,

Assistant Physician, General Hospital, Birmingham.

Physician, Children's Hospital, Birmingham.

A preliminary investigation of the distribution of rheumatic infection in Birmingham during the years 1922-1926[1] shewed that the great majority of cases occurred in houses situated along the courses of two streams running through the city. From this fact it was inferred that damp in dwelling-houses might have a powerful influence in predisposing towards rheumatic infection.

The establishment of a Rheumatism Bureau at the Children's Hospital under the care of the Lady Almoner, Miss N. J. Herald, has secured information concerning a larger number of cases. Including the four hundred children considered in the previous personal investigation the Bureau has now records of over 800 cases of rheumatic infection occurring in Birmingham in the period 1922-1927. Notifications of the cases have reached the Bureau mainly from the School Medical Service (by the kindness of Dr. G. A. Auden), and from the Staff of the Children's Hospital, both from the out-patient department and from the wards: a few have come from general practitioners.

I have satisfied myself that the notifications from the School Medical Service represent true cases of rheumatic infection: the majority of them were obvious instances either of chorea or carditis. The cases from the Children's Hospital can, of course, be accepted as definite: and those notified by general practitioners are also reliable; usually they have been children with severe carditis or chorea whom it has been impossible to control satisfactorily at home.

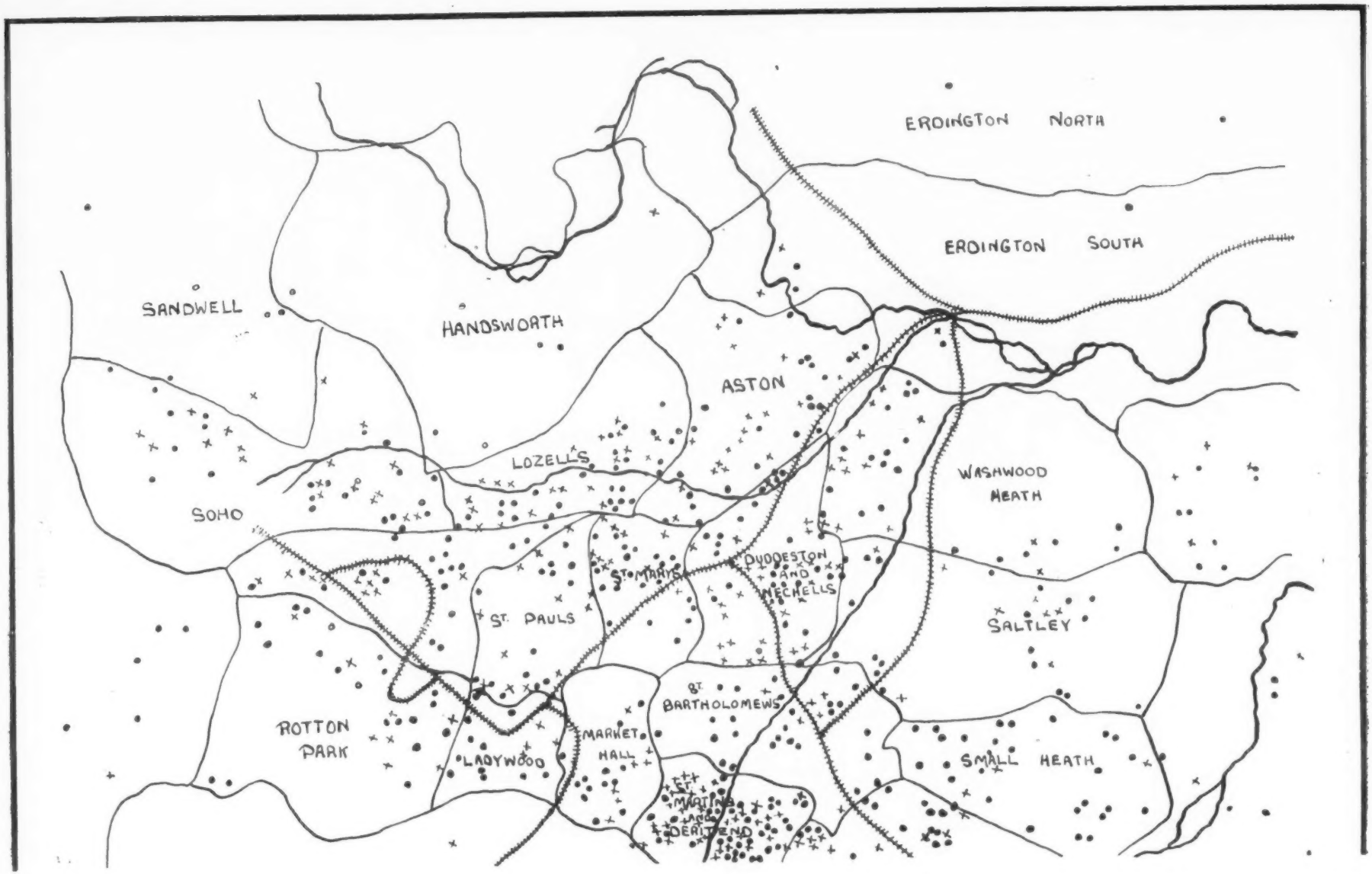
Since 1918 the housing shortage in Birmingham has been so severe that it has been impossible for the great majority of the working class population to move their homes and it may fairly be claimed that, as a rule, the houses in which rheumatic children were living at the time when they were notified to us were actually the houses in which they had acquired their disease. This contention could certainly be established up to the year 1925: since then removals may have introduced a fallacy, but I feel that it is only a slight one for we have been on our guard and have, as far as possible, enquired for recent changes of residence.

A spot-map to shew the distribution of 805 cases in the city has been prepared (Fig. 1), and on the whole it supports the conclusion reached in my earlier study, namely, that the majority of the cases crop out along the two streams that pass through Birmingham. It is also clear that there is no distinct regional distribution of chorea and rheumatism : the cases are indiscriminately mixed.

The fact that in Birmingham the proximity of working-class houses to water courses is apparently associated with a heavy incidence of rheumatic infection does not of itself warrant the inference that a damp house is of importance in the causation of the disease. There are obvious sources of fallacy which require consideration. It is possible, for instance, that the rheumatic zones as shewn in the map by mere chance correspond either with the areas of densest population or with those of greatest poverty.

TABLE.

Rheumatic Incidence	Wards.	Total (notified) case rate per 1,000. Rheumatic Infection. 1922-27	Population per acre.	Annual case rate per 1,000. Scarlet Fever 1924-26	Annual case rate per 1,000. Measles. 1917-19
Very High	St. Martin's & Deritend	2·0	109	1·98	14·4
	Balsall Heath	1·98	99	1·69	12·9
High	Market Hall	1·4	56	1·41	12·0
	Aston	1·2	79	2·00	15·6
	St. Mary's	1·2	98	1·87	15·3
	Ladywood	1·1	100	2·18	11·3
	Yardley	1·1	7	3·12	18·4
	All Saints	1·0	87	2·14	14·1
Moderate	Saltley	0·95	28	1·96	12·5
	Small Heath	0·92	46	1·91	14·5
	Sparkbrook	0·92	60	2·07	14·7
	Washwood Heath	0·9	30	1·94	12·0
	Rotton Park	0·8	65	2·65	15·1
	Handsworth	0·8	41	1·58	12·9
	Duddleston & Nechells	0·8	73	1·32	18·9
	Lozells	0·7	95	1·89	15·2
	St. Bartholomew's	0·7	67	2·64	16·3
	St. Paul's	0·7	82	1·84	15·5
Slight	Sparkhill	0·43	10	1·75	11·9
	Acock's Green	0·43	14	1·88	17·8
	Soho	0·4	39	1·19	14·5
	Selly Oak	0·4	17	2·59	13·9
	Sandwell	0·4	14	1·40	15·6
	Harborne	0·4	8	2·56	14·5
	King's Norton	0·4	8	2·06	9·6
	Edgbaston	0·4	14	1·51	7·9
	Moseley	0·36	10	1·52	15·7
	Erdington South	0·18	8	1·97	12·8
	,, North	0·05	11	2·10	11.1
	Northfield	0·0	2	1·57	16·2


ERDINGTON NORTH
ERDINGTON SOUTH
SANDWELL
HANDSWORTH
ASTON
LOZELLS
SOHO
WASHWOOD HEATH
DUDDESTON AND NECHELLS
ST. MARYS
ST. PAULS
SALTLEY
ST. BARTHOLOMEWS
ROTTON PARK
LADYWOOD
MARKET HALL
SMALL HEATH

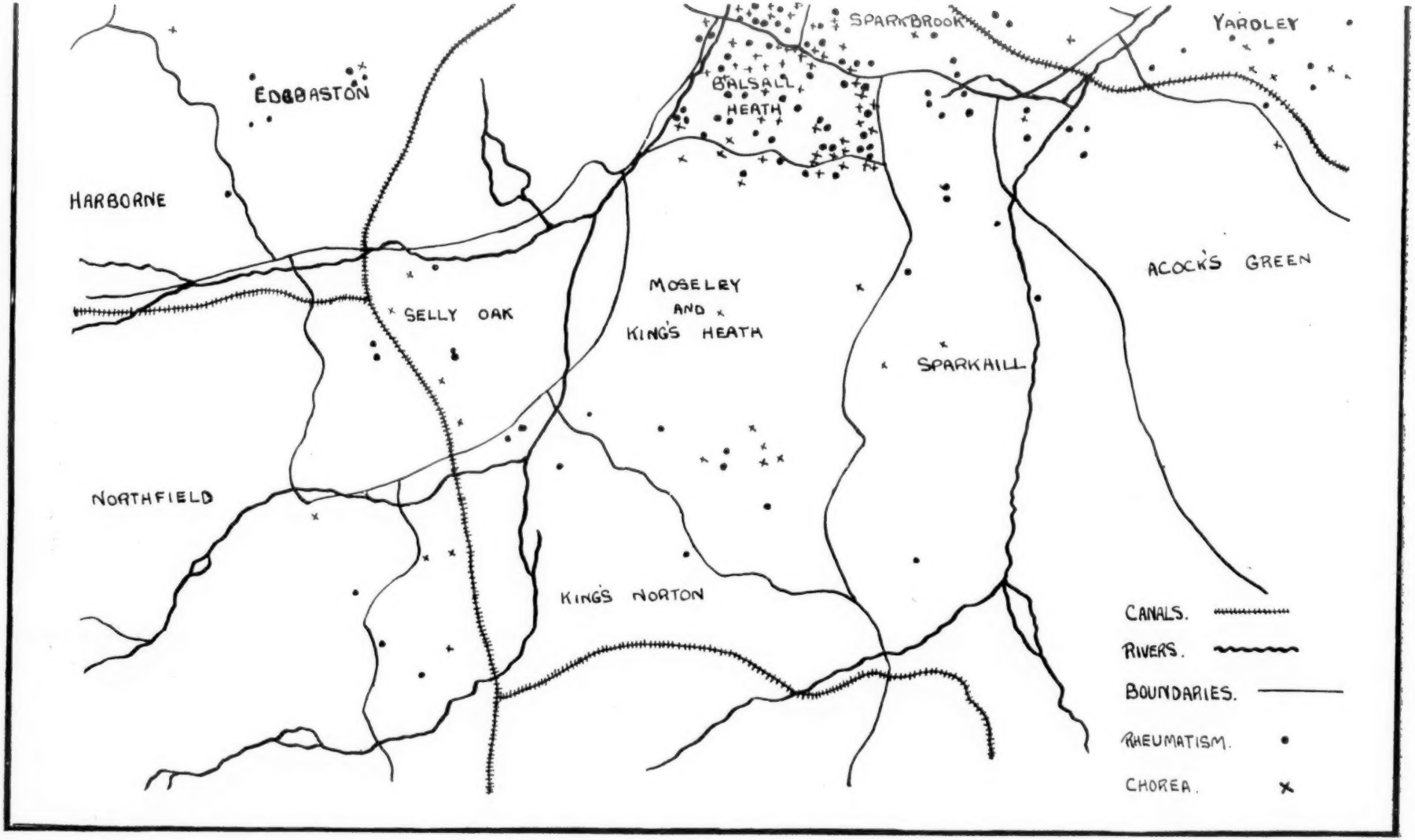


Fig. 1. Distribution of 805 cases of Juvenile Rheumatic Infection in the City of Birmingham. Rivers, canals and ward-contours are shewn. Streets have been omitted, but the cases are in their correct positions according to their street-distribution.

The Influence of Density of Population.

To explore the matter further I have prepared a table (p. 21), which shews the separate wards of the City of Birmingham together with the population per acre of each, and the total notified case-rate per 1000 of rheumatic infection during the years 1922-1927: in addition, for purposes of comparison records of the case-rates of measles and scarlet fever are included though, unfortunately, they are not available for the same years. I am indebted to Dr. W. H. Davidson, Senior Assistant Medical Officer of Health of Birmingham, for these figures.

Investigation of the distribution of a disease by studying its incidence in separate wards is not very satisfactory, for the divisions between the areas are purely arbitrary and a single ward may contain varied types of houses and social classes: for these reasons a table of this kind must be cautiously used, particularly when, as in this instance, the cases considered are only a proportion of the total number. Nevertheless no other statistical method seemed possible.

The maximum notified case-rate per thousand of rheumatic infection in a single ward is 2, and I have arbitrarily divided the table into four sections containing wards with very high (2·0—1·5), high (1·5—1), moderate (1—0·5), and slight (0·5—0) incidence of the disease.

There is on the whole a broad relationship between the incidence of rheumatism and density of population. Thus in the last section of wards with slight incidence there is none with dense population, and in the wards with very high and high degrees of rheumatic infection there is only one ward with sparse population (Yardley). It is clear, therefore, that the distribution of rheumatism among wards in the City of Birmingham supports the view that the prevalence of the disease is favoured by urban conditions and density of population. Study of the third group of wards, those with moderate incidence of rheumatic infection, indicates clearly, however, that some other factor, or factors, must play an important part, for there are included in it a number of wards in which, with a population as dense as that of the first two groups, the case-rates are much less. Why, for instance, should Lozells have one-half the rheumatic case-rate of Aston, and St. Mary's double that of St. Pauls? Saltley and Washwood Heath, again, are not densely populated and yet they have high rheumatic incidence.

It is further worth recording once more the fact that on investigating the housing conditions of an unselected group of rheumatic children in Birmingham I found no evidence of relative overcrowding; the figures were those common in the areas in which they lived[1].

The Influence of Poverty.

It is possible that degrees of poverty may be responsible for these curious variations and the matter deserves consideration despite the general impression derived from hospital practice, that the majority of rheumatic children do not

belong to the destitute class. In his Annual Report for 1918, Sir John Robertson, the Medical Officer of Health for Birmingham, dealt particularly with the housing problem and one of his charts (Fig. 2) is here reproduced by his permission. This shews the relative distribution of back-to-back houses in the wards of the City. If this chart be taken as a fair indication of the degree of poverty existent in various areas, as I think it may, and if it be

Fig. 2. PERCENTAGE OF BACK-TO-BACK HOUSES: CITY OF BIRMINGHAM, 1918.

51—76 per cent.
27—47 „ „
13—14 „ „
0·1—8 „ „

compared with one of a similar type (Fig. 3) to shew the notified case-rate of rheumatism it will be at once apparent that poverty and rheumatism are not closely associated in their distribution. Balsall Heath, a ward with relatively good housing has a great incidence of rheumatism; St. Paul's, one of the central ring of slum areas which strangle Birmingham, has only a moderate rheumatic case-rate.

The Influence of other Infectious Diseases.

It seemed possible that predisposition to rheumatism might be due to the ncidence of other infectious diseases. Reference to the table (p., 21) shews that,

Fig.3. INCIDENCE OF RHEUMATIC INFECTION: 805 CASES IN THE WARDS OF THE CITY OF BIRMINGHAM, 1922-1927.

2—1·5 per 1,000
1·5—1·0 „ „
1·0—0·5 „ „
0·5—0·0 „ „

so far as figures are available, they give no support to this hypothesis in the case of scarlet fever and measles. The incidence of diphtheria (the figures for which were given to me by Dr. W. H. Davidson) is also not related.

The Influence of Subsoil and Surface Water Level.

The nature of the subsoil and the surface water level are matters of possible importance. Unfortunately it is very difficult in Birmingham to obtain information on these points and the matter is one for future investigation.

Conclusions.

The conclusion from this study, that neither density of population, nor poverty of housing, nor incidence of some other infectious diseases account satisfactorily for the variations of the rheumatic case-rate in different parts of the city, gives additional significance to the tentative opinion derived from the spot map (Fig. 1) that the situation of working-class houses close to water courses is of considerable importance. There are two points in connection with the map which merit consideration. First, the number of cases in Ladywood which is at some distance from the rivers is considerable. These cases represent in the main recent notifications to the Rheumatism Bureau of the Children's Hospital, itself situated in the middle of this area. It is possible, I think, that the large number of cases charted in this situation is due to the fact that delicate children in Ladywood are frequently taken direct to the hospital close by, and diagnosis and notification are in consequence likely to be more thorough and frequent. A fallacy of this kind is certainly possible when the system of notification is incomplete.

The second difficulty in accepting the view that the situation of the water courses largely determines the incidence of rheumatic infection is the fact that there are a large number of cases in part of Balsall Heath, towards Sparkbrook, which is well away from the river and also lies on high ground. The only hypothesis that occurs to me to account for this fact is that children in this area may be specially liable to infection by contact in schools with those living along the river banks.

REFERENCE.

1. Thomson, A. P., Birmingham Med. Rev. 1926, N.S., I. 1.

A REVIEW OF 180 CHILDREN SUFFERING FROM RHEUMATISM, CHOREA AND CARDITIS.

BY

ROBERT MARSHALL, M.D., F.R.C.P.I., D.P.H.

Physician, Ulster Hospital for Children & Women:

Assistant Physician, Royal Victoria Hospital, Belfast.

This paper represents the result of an attempt made at the Ulster Hospital for Children and Women to take stock of what knowledge has been gained of a series of 180 children attending the Hospital for one or more of the triad, rheumatism, chorea and carditis.

TABLE I.

ANALYSIS OF 180 CASES OF RHEUMATISM OR CHOREA IN CHILDREN.

	Group.				
	A	B	C	D	E
Number of Cases	79	16	24	34	27
Average Age	8·9	11	9	9·4	8·8
Males	34	5	7	18	10
Females	45	11	17	16	17
Social Grouping—					
(1) Particularly thrifty and industrious parents	8	0	1	1	1
(2) Ordinary "working-class" parents	45	11	10	20	12
(3) Very poor parents	26	5	13	13	14
Referred by School M.O.	21	2	3	3	0
In-patients (U.H.C.W.)	42	11	16	8	12
Aver. No. of weeks in Hosp.	6	9	9	7	7
Family History of Rhc. Infection	10	0	1	4	1
History of Acute Rheumatism	26	0	—	6	—
Less acute pains in limbs	44	16	—	28	—
Tonsillitis	27	9	10	17	10
Tonsils removed	11	3	7	7	5
Transient apical systolic murmur	0	0	0	5	4
Mitral Regurg. without Stenosis	49	9	17	—	—
Mitral Stenosis	18	5	5	—	—
Mitral and Aortic Lesions	9	1	0	—	—
Pericarditis	8	2	0	—	—
? Myocarditis only	3	1	2	—	—
Sinus Arrhythmia	1	0	1	10	4
Cardiac Lesion not severe	22	2	5	—	—
Cardiac Lesion severe	57	14	19	—	—
Died	9	2	2	0	0

Group A: Rheumatism and Carditis.
Group B: Rheumatism, Chorea and Carditis.
Group C: Chorea and Carditis.
Group D: Rheumatism, with no evidence of Carditis.
Group E: Chorea with no evidence of Carditis.

For this purpose I have arranged the series in five groups (*vide* Table I):

Group A. 'Rheumatic' children with evidence of carditis.
Group B. Children who have had limb-pains, chorea, and carditis.
Group C. Children who have had chorea, and carditis, but no limb-pains.
Group D. Children who have had limb-pains, but show no evidence of carditis.
Group E. Children who have had chorea, but neither limb pains nor evidence of carditis.

Group A. (*Rheumatism and Carditis.*)

This is the "rheumatic" group: all these children have suffered more or less severely from rheumatic pains. The average age of first attendance at Hospital was almost 9 years: the majority were girls. I have attempted, with the aid of the Sister-in-charge of the Out-Patient Department, to divide them into three groups according to the economic position of their parents; I am satisfied that all were suitable for hospital treatment, but some were better off than others. It will be seen that most were graded in the second group of ordinary working class parents, more or less regularly employed.

42 of these children were in-patients and the average duration of their stay in Hospital was six weeks.

In 26 cases there was a history of a rheumatic attack of such severity as to keep the child in bed: 44 had pains varying from slight so-called growing pains to something short of true acute rheumatism: in the remaining 9, while there was evidence of rheumatic toxæmia, such as lassitude, pallor and loss of weight, pain was slight or absent. I have kept no record of the frequency of rheumatic nodules. 27 had tonsillitis recorded in the notes, and in 11 of these tonsillectomy was performed: in some cases the parents declined consent, and in some the severity of the cardiac condition was a deterrent. Broadly speaking I think that those who were operated on benefited by it.

The commonest valvular lesion, as might be expected, was mitral regurgitation: 49 cases, as compared with 18 in which there was stenosis, and 9 in which there were mitral and aortic lesions. Only two of these children had no evidence of valvular lesion on first reporting to hospital: in all the others the valvular lesion was already obvious and some damage already done. One of these two children (No. A.8) was admitted in 1924 for 4 weeks, 3 days after the onset of joint pains: her heart was apparently normal when she left Hospital. On being sent for in December, 1926, for re-examination, she had had no recurrence, she had no symptoms, her electrocardiogram was normal, but a short apical systolic murmur strongly suggested that carditis had occurred. The other child was at first considered to be a purely myocardial case, but, when she last reported at hospital after a long interval, she was found to have developed a mitral lesion.

Of the 9 cases where a diagnosis of pericarditis was made, only one showed involvement of the pericardium without evidence of endocarditis. This was a very acute case which cleared up rapidly and has not, to my knowledge, recurred.

The 3 cases on whom I have made a provisional diagnosis of myocarditis only are as follows :—

Case 1. A.9 : male *æt.* 14 years. Tachycardia noted at each examination from 1924 till 1927 ; rate varies from 132-144 ; hæmic murmur over base ; electrocardiogram shows inversion of T wave in lead 3.

Case 2. A.13 : female, *æt.* 10 years. In Oct., 1926, admitted as a cardiac suspect ; history of tonsillitis, slight pains ; had tonsillectomy performed, December, 1926. Pulse rate persistently rapid. Ecg. in December, 1926, and January, 1927, showed only inversion of T wave in lead 3, but on 4th November, 1927, T wave in lead 2 was noted to be flattened. This is the only case in this series in which I have observed flattening of T in lead 2. (Figs. 1 and 2.)

Case 3. A.38 : Dr. Simm's patient, male, *æt.* 6. This boy has no obvious valvular lesion, but has frequent and persistent ventricular extra-systoles, marked inversion of T III, and his cardiogram is of left ventricular predominance type. He has also clinical and X-ray evidence of tracheo-bronchial adenitis. His tonsils were large and have been removed. His mother says he is " in the best of health " after a long course of sodium salicylate, but his arrhythmia and his electrocardiogram are unchanged. (Fig. 3.)

These cases, where there is no obvious endocarditis, are at once difficult and interesting, and I hope to watch their development.

Of the 72 cases examined by the electrocardiograph, 33 showed normal records. The majority of these were cases of early and uncomplicated mitral regurgitation. Four cases of mitral stenosis showed normal cardiograms, and so did 3 cases of aortic regurgitation with mitral regurgitation and stenosis. I suppose that in these last cases the balance between the two ventricles, both of which are enlarged, has been maintained in normal ratio. I think that these are the relatively favourable cases of mixed aortic and mitral lesion.

I have kept separate from these the 9 cases in which the record was normal except for inversion of T in lead 3. While it is universally recognized that inversion of T in leads 1 and 2 is " a sign of ill-omen " and indicative of serious myocardial change, there is still uncertainty as to the reason why the T wave in lead 3 may be inverted in records of hearts that are otherwise normal.

The question of right and left ventricular predominance is not any simpler. In this group, 4 children showed right ventricular predominance to a greater or less extent ; two had mitral stenosis, two mitral regurgitation ; one of each

TABLE II.

Electrocardiographic Results.

Electrocardiograms.	A	B	C	D	E
Cases examined	72	10	18	15	8
Normal	33	4	9	13	6
Inverted T in lead 3	9	1	3	2	2
R. V. predominance	4	1	1	—	—
L. V. predominance	11	1	5	—	—
Large or notched P wave	10	2	2	—	—
Extra-systoles only	2	1	1	—	—
Aur. fibrillation or flutter	2	—	—	—	—
Long P-R interval	1	—	—	—	—

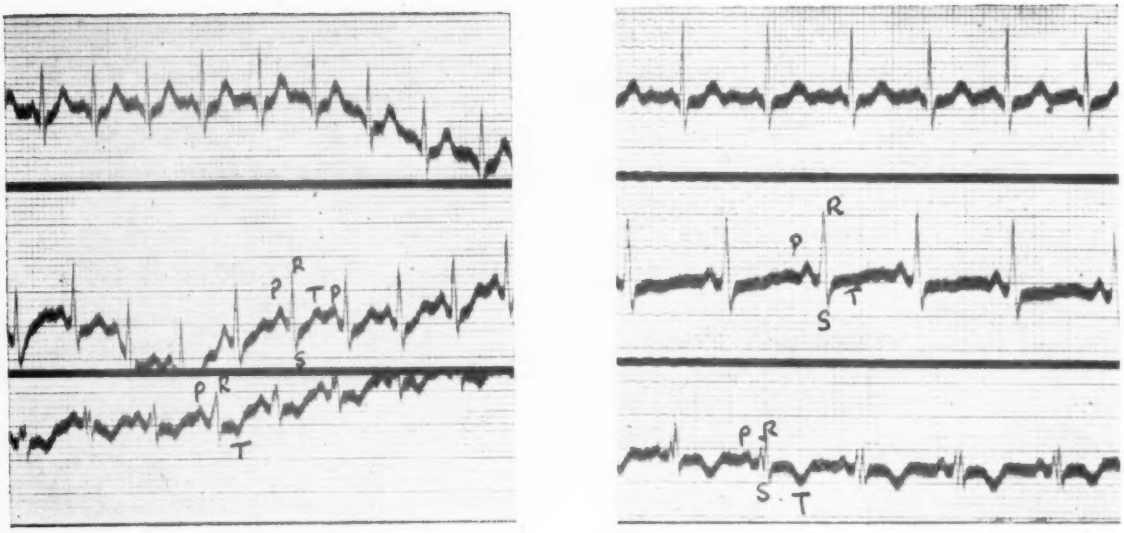
kind is dead. Both of the survivors have been X-rayed and in each case the report is "heart enlarged both to right and left." As compared with these four cases, 11 cases showed evidence of left ventricular predominance. I was at first surprised at this in view of the frequent involvement of the mitral valves as compared with the aortic. It is, however, in accordance with what Pardee[1] of New York has found. He says: "Mitral stenosis leads to an hypertrophy of the right ventricle through a damming back of blood in the pulmonary capillaries, thus increasing its work. Mitral regurgitation does this also though secondarily and only after overtaxing the left ventricle. Hence the earliest records with this valve lesion may show a left ventricular predominance, later ones giving a normal Q.R.S., and later still, as stenosis develops, a right predominance." Of the 11 cases of this left ventricular type four had aortic regurgitation, five had mitral regurgitation, one had pericarditis without obvious endocarditis and one was the case of Dr. Simm's, No. A.38, whom I have already described as a case of myocarditis. The X-ray findings were as follows: 8 were X-rayed and in 7 of these the heart was described as being enlarged, principally to the left side, and in 1 the description was "heart generally enlarged."

Two additional factors must, of course, be borne in mind. First, ordinary radiography of the chest gives some degree of distortion of the size and shape of the heart. This can only be obviated at considerable expense by the installation of an orthodiagraph or of so powerful a plant as to enable the radiographer to expose his patient to the rays at a distance of more than seven feet from their source. There is this defence to the ordinary method, that the children are all radiographed with the same technique and the degree of distortion is more or less the same for all.

The other factor is that the heights of the R and S waves, by which predominance of one or other ventricle may be indicated, are also affected by the anatomical position of the heart in the chest and in particular by the position of its electrical axis. Pardee[1] sums up his consideration of the facts by stating that "in general, this electrocardiographic sign . . . is found to be correct and especially if there are evidences of cardiac enlargement . . . the clinical pathological studies so far reported correlating the electrocardiographic predominance with the relation of the ventricular weights show that in 75% of instances, the electrocardiogram will suffice to place the ventricular relations."

As might be expected, enlargement or notching of P, indicative of auricular overaction was a relatively common finding, occurring in 10 cases, all of which had mitral involvement. Only two records show extra-systoles, though these were sometimes detected clinically in other cases.

There were two cases of delirium cordis: one a girl, (A.63) of 13 years (Fig. 5) who has auricular fibrillation varied by periods of flutter, and the other a girl of 5 (A.67) who was admitted with a tachycardia of 200 per minute, due I think to 1 in 1 flutter; this child died soon afterwards. On commencing this enquiry I expected to find many more cases of rheumatic heart block, but in only one case in this group did I find a prolonged P-R



Figs. 1 and 2. Case No. A. 13. R.T. Female æt. 9.

First electrocardiogram (3/12/26) showed inversion of T in lead 3 only. Last electrocardiogram (4/11/27) showed inversion in 3, and flattening in lead 2. Heart persistently rapid (ca. 144). X-ray: Heart normal in size.

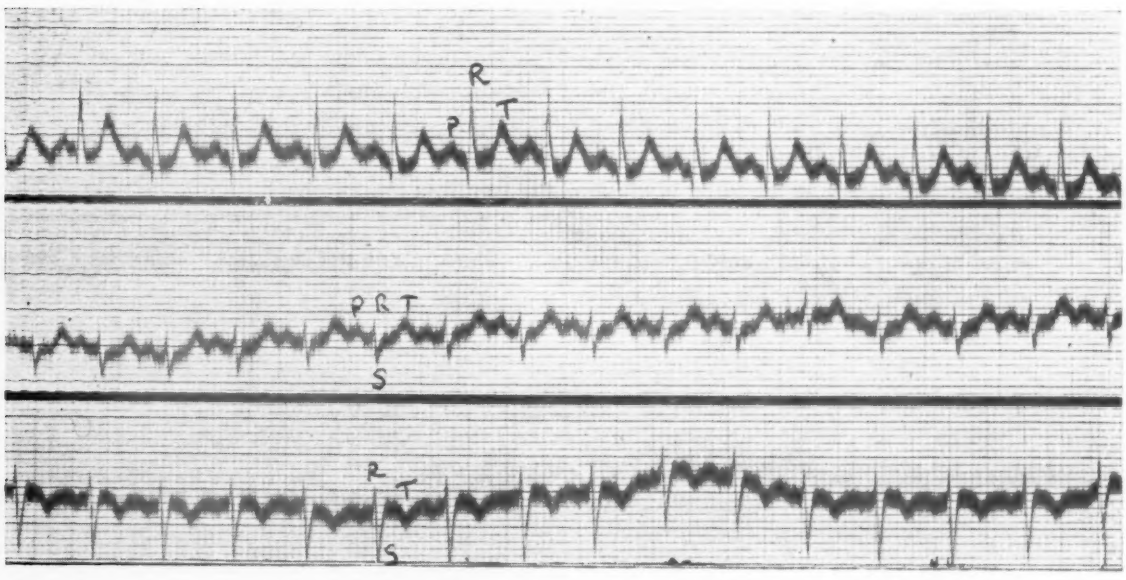


Fig 3. Case No. C. 22. Male æt. 11.

Chorea, treated in U.H.C.W. Heart apparently normal. Electrocardiogram: Of type associated with left ventricular predominance. Inversion of T in lead 3. X-ray: Heart enlarged generally and to left.

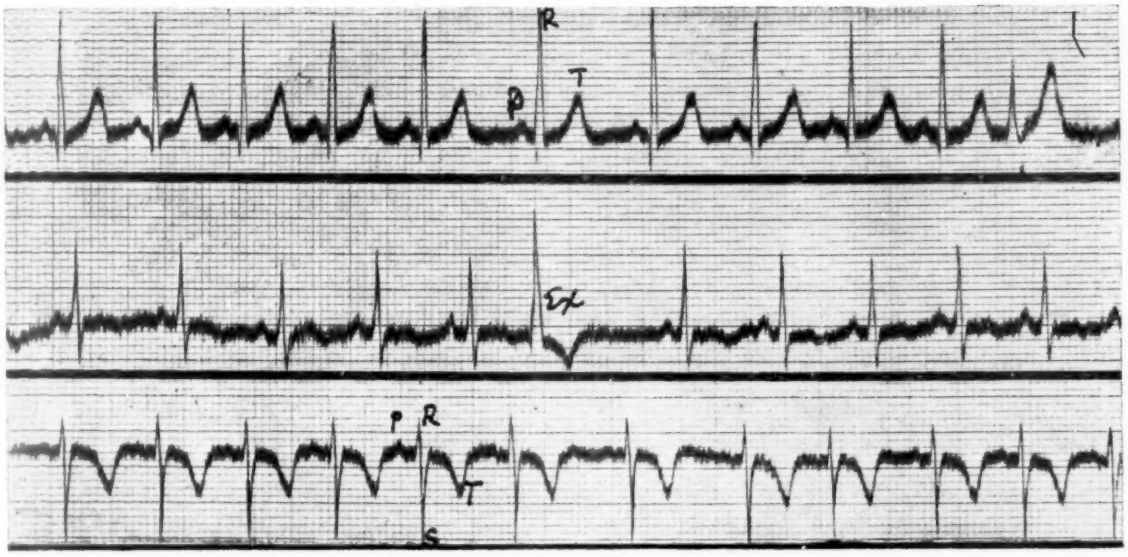


Fig. 4. Case No. A 38. T.K. Male æt. 6.

Electrocardiogram: One extra-systole is seen in lead 2. The high R in lead 1, together with the deep S in lead 3, suggest left ventricular predominance. X-ray: Root shadows increased; peribronchial fibrosis; ?? early T.B.

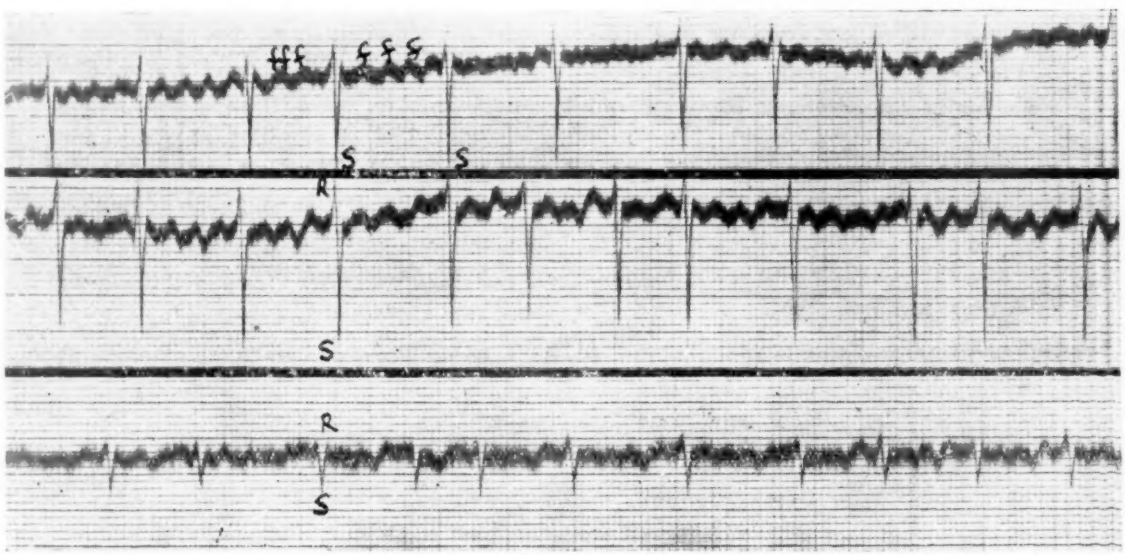


Fig. 5. Case No. A 63. B.W. Female æt. 13.

History of "Growing Pains." Mitral Regurgitation. Electrocardiogram shows auricular fibrillation with periods of flutter. X-ray: Heart enlarged to right and generally.

interval. This boy (A.34) had a P-R interval of 0·2 sec. which is about the normal maximum interval; he had a hypertrophied heart and mitral stenosis with a tendency to tachycardia.

I should like to emphasize the importance of the observation that of these 79 children, only one is noted to have sinus arrhythmia. This bears out Sir James Mackenzie's[2] dictum that it "is a sign of a healthy heart muscle," but like almost every other sign in medicine, there are exceptions and its presence does not constitute absolute proof that the heart has escaped rheumatic attack.

The classification into slight and severe heart disease is at best only conjectural, but is in itself evidence of the serious problem which confronts us. If I am right, of these 79 children 57 have a serious, crippling, and ultimately fatal disease of the heart. Of these 9 are already dead.

Group B. (*Limb-pains, Chorea and Carditis*).

This is a smaller group, but it presents a still more serious problem, as rheumatism of the limbs together with chorea appear to represent a still more serious infection. It will be seen that girls were still more frequently the victims, that a larger proportion were in-patients, and for longer periods. Every one of these children had evidence of carditis when first seen at hospital, and in seven at least the heart lesion is now more serious than when first observed. Three are known to have had slight recurrences of chorea, and three have had slight pains in the limbs since first coming under treatment. It is regretted that only three of the nine who had tonsillitis have had their tonsils removed. I think the main reason for this is that one hesitates to recommend tonsillectomy while the choreic movements persist, and when they are better the parents do not wish the child to be re-admitted for operation. Mitral lesions predominate, as the table shows, and I have diagnosed as myocardial a case where a boy (B.16) has a large heart on X-ray examination, with left ventricular predominance by electrocardiograph, but no obvious murmur.

There was nothing remarkable in the electrocardiograms: the case showing evidence of right ventricular predominance was one of mitral regurgitation and the X-ray report was "heart enlarged to right." No single case of the series had persistent sinus arrhythmia; one girl had it in the earlier days of her carditis but it disappeared. Fourteen are provisionally classified as severe cases of whom two have died. One of these died in hyperpyrexia during her first attack of acute chorea. The other had rheumatism, acute chorea and pericarditis; she left hospital apparently doing well but died some months later.

Group C. (*Chorea, Carditis, no limb-pains*).

This group is of the children in whom was elicited no history of limb-pains, but who had chorea and heart trouble. Females again are in the majority, and 16 of the 24 were treated as in-patients. All 24 would have been in-patients, if they had been seen during their first attack and their parents had been willing. Two of the children gave a history of an attack precipitated by emotional stimulus, grief or fright. There were 5 cases of mitral stenosis,

seventeen of mitral regurgitation, and two, diagnosed as in Groups A & B as myocarditis on the grounds of a left ventricular predominance (Fig. 3) together with an X-ray finding of hypertrophy. I wish to make it clear that I am not dogmatic about this type of child, but only that I cannot classify it as having no evidence of carditis.

TABLE III.

FREQUENCY OF CHOREIC ATTACKS.

Number of Attacks of Chorea.	Group B	Group C	Group E
One attack only	13	13	22
Two attacks	2	5	4
Three „	0	4	0
Four „	1	1	1
Five „	0	1	0

Three others showed records of this left ventricular type but have endocarditis: two have mitral regurgitation and one has mitral stenosis. One girl (No. C.8) had mitral stenosis with right ventricular preponderance. She has since died.

The case showing sinus arrhythmia is interesting:

No. C. 20, a girl, *at.* 11, came to hospital in March, 1925, during her third attack of chorea. She had a rough apical murmur strongly suggesting early stenosis. She has been seen at frequent intervals since; her cardiac condition is no worse, and she still has sinus arrhythmia.

Nineteen of the twenty-four have been classified as having severe heart lesions, and of these two are already dead.

Groups D (limb pains alone) and E (chorea alone).

I do not propose to give detailed descriptions of these cases. In some cases a systolic apical murmur was recorded, and this disappeared. I cannot express an opinion whether this was caused by a carditis so slight as to leave no obvious valvular lesion in its train. It seems to be the case that the appearance of an apical systolic murmur in a rheumatic child does not necessarily mean that he is doomed to cardiac disablement. Twenty-six cases of group D, and twenty of group E have been re-examined within the past three months.

I find it difficult to assess the severity of the rheumatic pains or the chorea in these non-cardiac cases as compared with groups A, B & C. Some of the choreic cases were certainly very severe; seven of them should perhaps have been grouped apart, as they had limb pains as well as chorea, but usually slightly. It is noteworthy that many severe cases of chorea, with frequent recurrences, never develop carditis, and one sometimes wonders if this is due to a different causative agent.

SUMMARY.

On a general re-survey of the 5 groups, one notes the absence of any case of a purely aortic lesion without mitral involvement; the comparative frequency of evidence of predominance of one or other ventricle, sometimes without obvious endocarditis; the fact that right ventricular predominance in childhood is apparently of serious prognostic significance (three of the six cases in which it appeared are already dead); that fourteen out of 61 "non-carditic" children showed sinus arrhythmia, but only 2 out of 119 cases of heart disease; and, most significant of all, that in all but two of the cases of valvular disease of the heart, the presence of a murmur was noted on the hild's first visit to hospital.

TREATMENT.

All, or almost all, of these children have been treated by the administration of sodium salicylate with twice its weight of sodium bicarbonate, and, where the parents co-operated, this was continued for many months, varied from time to time with iron, usually in the form of the syrup of the iodide. "Rheumatism is a smouldering fire" as Poynton said, and I am inclined to the belief that it is during the smouldering stage as much as during the acute conflagration that sodium salicylate is indicated. I admit that Poynton[3] states that "his experience of salicylates is so unsatisfactory that . . . in the most formidable cases of carditis in the young his best results have been obtained without their use."

Carey Coombs [4] on the other hand states that "often it is an advantage to prolong its administration after discharge from hospital". His own experience leads him to the belief that the administration of salicylate does limit the extent of the cardiac lesions, probably by attacking the micro-organisms somewhere between their portal of entry into the circulation and their final settlement in the cardiac tissues. No other drug has a similar action: to that extent therefore salicylate is a specific for rheumatic infection. Lutenbacher[5] of Paris gives large doses for 15-20 days after the temperature of acute rheumatism has fallen and continues the administration of the drug for 12-18 months after the apparent cessation of all symptoms. Kerley[6] of New York gives 10 grains daily for 5 days in each 15, for 6 months, and for 5 days in each 30 for a further 6 months. Parkinson[7] advises its administration for many weeks after an attack, especially during the winter months, with iron and cod liver oil as accessories. Miller[8] who has enquired very closely into this matter says that he believes that the more freely and persistently we use salicylate in the earlier rheumatic attacks the less often we shall be faced with dreadful failures.

I think it *must* be an argument in favour of this method of treatment that only two of these Ulster Hospital children have developed a definite endocarditis who were free from murmurs when they first came under treatment, and it *may* be a reason why nine had only transient murmurs.

While emphasizing its importance I do not wish to minimize the value of other aspects of treatment : rest in bed during any rheumatic manifestation and for some time afterwards is of primary importance. As a rule I think these children, particularly the chorea cases, can be nursed better in hospital than in their own homes. Of these 180 children, 89 were in-patients, representing 645 weeks in the Ulster Hospital alone, at a cost of about £970.

My attitude to tonsillectomy may be summed up in the statement (I do not know its author) that "tonsils are as frontier forts which, when they have fallen into the hands of the enemy, are no longer a defence but a menace to our safety."

Dr. T. H. Davey in Sir Thomas Houston's Laboratory kindly examined a few of the tonsils after removal in the hope of finding the newly described bacillus cardio-arthritidis but without success.

This uncertainty as to the causative factor is the cause of difficulty not only in diagnosis and treatment, but in ascertaining when quiescence or cure has been reached, and this necessitates prolonged medical supervision.

In America the American Heart Association has done a great deal to educate public opinion about the importance of early symptoms. Near the larger cities in England and in America special country homes have been devoted to the after treatment of these children ; gradual physical exercises, education and vocational training are given according to the physician's recommendation. This last point is of the utmost importance. These children must be trained for sedentary occupations rather than be allowed to drift casually into heavy work for which they are not fitted.

In Bristol, Dr. Askins, the School Medical Officer has issued a circular letter to all School-teachers, warning them of the importance of growing pains, shortness of breath and nervous twitchings as evidence of rheumatism and potential heart disease. I think it is an excellent thing to encourage the co-operation of the school-teachers in this way.

In the Ulster Hospital, the Medical Staff is about to ask the Board of Management to print a leaflet of instructions to parents on the care of Rheumatic children. This leaflet is based on a similar one issued at Paddington Green Children's Hospital.

A series of cases such as this is an argument in favour of compulsory notification of rheumatism in children. This experiment is at work in parts of London and is an example which might well be copied in Northern Ireland, where comparison could then be made of its incidence in town and country. Country doctors seem to regard these cases as very rare in their practices, and this is apparently the experience of School Medical Officers in rural districts. The information gained by even an experimental year or two of compulsory notification would be invaluable, and would bring home to the profession and the public the prevalence of the disease. This has been well expressed by Poynton in his preface to Carey Coombs' book "Rheumatic Heart Disease." "Surely the time has come to turn to rheumatism and particularly acute rheumatism in the young. Such patients must have the sympathy of all, for none appeals more than the child with rheumatic heart disease who is the most

alert and engaging of all our patients. If ever a medical venture on a large scale was indicated in this country, it is the prevention of rheumatic heart disease, and by this the writer means the supervision and care of the rheumatic child, adolescent and adult."

I should like to express my thanks to my colleagues and to Miss Martin and Sister McCaughey of the Hospital for their invaluable help in various aspects of the work.

REFERENCES.

1. Pardee, *Clinical Aspects of the Electrocardiogram*, 47, 48.
2. Mackenzie, J., *Diseases of the Heart*, 3rd. Ed. 187.
3. Poynton, F. J., *Brit. Med. J.*, Lond., 1924, 986.
4. Coombs, C. F., *Rheumatic Heart Disease*, Bristol, 1924. 323.
5. Lutembacher, *Med. Sci. Abst. & Rev.*, Lond., VI, 97.
6. Kerley, C. G., *Practice of Pediatrics*, Philad., 2nd Ed., 723.
7. Parkinson, J., *Personal Communication.*
8. Miller, R., *Brit. Med. J.*, Lond., 1923, ii. 704.

HÆMORRHAGIC DISEASE OF THE NEWBORN.

BY

RUBY S. BEVERIDGE, L.R.C.P., M.R.C.S.

(From the Medical Department, Royal Hospital for Sick Children, Glasgow.)

In recent years there has been an increasing amount of literature on the subject of the forms of hæmorrhage occurring in the newly born. One of the rarest of these is the group known as "hæmorrhagica neonatorum," and consequently it may be of interest to record some facts ascertained during a survey of the case histories of 24 examples of this condition which have been under observation in the Royal Hospital for Sick Children, Glasgow.

Holt[1] applies the term "hæmorrhagica neonatorum" to "those cases in which the hæmorrhages are not associated with any other known processes, and in which the escape of blood from the smaller blood vessels is the chief or essential symptom." This definition excludes such varieties of neonatal hæmorrhage as are due to birth traumatism, asphyxia, syphilis, gastric or duodenal ulcer, and hæmophilia.

A curious characteristic of the disease lies in the spontaneous commencement and termination of the bleeding. It is noteworthy, too, that although present-day treatment will normally stop the bleeding, this result very often occurs naturally. Another interesting feature of the malady is constituted by the region or regions of the body that may be the seat of hæmorrhage. It would appear that the mucosa of the alimentary tract, the umbilicus, or the subcutaneous tissues, are the sites most frequently affected. The bleeding may be internal, external, or both combined. Post-mortem examination will, of course, reveal the presence of internal bleeding. It is an interesting fact too, that gross lesions, e.g., ulcers, are rarely found in cases exhibiting bleeding from the alimentary tract. Holt found post mortem in 24 cases of bleeding from the stomach and intestines ulceration of the gastric mucosa in 9 and of the intestinal mucosa in only 4 cases.

Aetiological Factors.

"Hæmorrhagica Neonatorum" is a disease of obscure ætiology. Well nourished infants are apparently just as liable to be attacked as the feeble or ill nourished.

It has been clearly established that it is not a manifestation of hæmophilia: the frequency with which females are attacked and the absence of any tendency for bleeding to recur, being quite sufficient to differentiate it from hæmophilia. The latter has been observed to occur rarely in infants under one year. Grandidier[2] in 1871 stated that in 185 bleeder families comprising 576 bleeders, only 12 infants were affected with hæmorrhage at the separation of the umbilicus.

Capon[3] regards it as unlikely that birth traumatism plays a part in the causation of this disease. Formally sepsis was noted to be often associated, and this gave rise to a theory of a possible infective origin, a view favoured by Townsend[4]. Nowadays, however, sepsis neonatorum is rare and is not considered to play any part in the causation.

Syphilis has been recorded as an associated factor in a relatively small proportion of cases. Hess[5] collected some instances relating to this point with a view to determining the question "are we dealing with syphilis hæmorrhagica or a secondary infection of a syphilitic infant?" Hess's own case was that of a female infant with the onset of hæmatemesis and melæna on the 6th day, subcutaneous hæmorrhages and death on the 7th day. At the post-mortem examination the child was jaundiced, with exfoliation of the skin of the hands and feet: hæmorrhages were found in the stomach and bladder, and histological examination revealed interstitial changes between the lung alveoli, and also cirrhosis of the liver. In one of a series of 13 cases of spontaneous hæmorrhage of the new-born recorded by Abt[6] there was a history of the mother having contracted syphilis during pregnancy. The child weighed 3½ lbs. at birth and lived one hour only. Autopsy revealed hæmorrhages into the peritoneal and pleural cavities. In another case in Abt's series there was no history of syphilis, but it was suspected on account of the premature birth of the infant and the presence of pulmonary atelectasis and pneumonia. Hæmorrhages were found in the lungs, skin, thymus, thyroid, liver, stomach, intestine, suprarenals, spleen and pericardium. Hess, summing up these cases with several others from the literature, concluded that "syphilis is undoubtedly an important factor, in some acting as a direct cause due to changes in the vascular system, not alone on the blood-vessel walls but on the blood as well."

Modern research has been concentrated on the examination of the blood in these cases in order to ascertain if the essential cause of the disease lies in some defect in the blood constituents. Rodda[7], in an extensive study of the coagulation and bleeding times in the newly born, shows that in cases of idiopathic hæmorrhage these times are invariably prolonged beyond the normal. According to his method of determination the normal coagulation time ranged from 5 to 9 minutes, with an average of 7 minutes, whereas in cases of hæmorrhagica neonatorum there was a prolongation to 20, 30 or even 90 minutes, with a corresponding prolongation of the bleeding time. Rodda further demonstrated that in the normal infant "the coagulation time varied on different days of the infant's life, showing a tendency to prolongation over the 2nd, 3rd and 4th days, with a maximum on the 5th day, and a return to the time obtained during the first 24 hours before the 10th day." The average bleeding time was 3½ minutes, with a range of 2 to 5 minutes.

Through the kindness of Dr. G. B. Fleming I have been enabled to test the coagulation and bleeding times of newly born infants at the Glasgow Maternity Hospital, and thus to investigate this question for myself. None of these infants presented during the time of study any evidence of hæmorrhage. The apparatus used was that devised by Gibb[8], and employed as he recommends. For obtaining blood the skin was punctured by a spring lance as used by Rodda. Gibb found that in adults the average coagulation time was 97 seconds. The figures obtained by this method in the newly born are shown in Table I.

TABLE I.

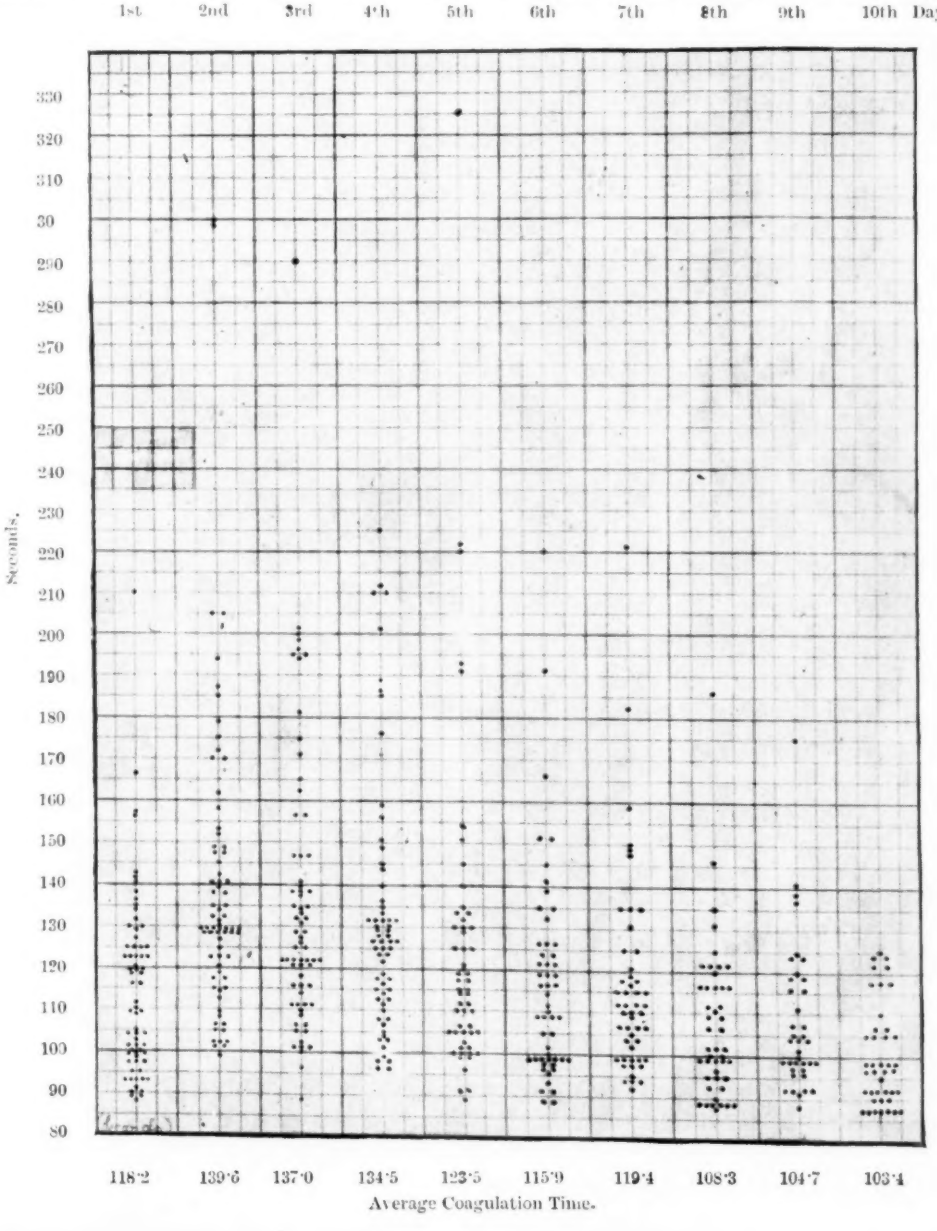
Observations on Blood Coagulation in the New Born.

Age in Days ..	1	2	3	4	5	6	7	8	9	10
Average coagulation time (seconds) ..	118·2	139·6	137·0	134·5	123·5	115·9	119·4	108·3	104·7	103·4

Average bleeding time, 2½ minutes.

The individual results as seen in the Chart below show a fairly wide variation but the averages show a definite rise in the coagulation time on the 2nd, 3rd and 4th days, and thereafter a fall to below that of the level of the 1st day.

Fig. 1. Chart showing Distribution of Coagulation Time in Normal Infants from 1 to 10 Days.



It is interesting that in hæmorrhagic disease of the newly born the onset of the bleeding is most frequent during the first week in life, and its greatest incidence is from the 2nd to the 5th day, thus corresponding with the period in which there is normally prolongation of the coagulation time. Capon has in consequence suggested that the pathogenesis may in part be dependent on a delay in reaching the normal level.

The exact nature of the element here lacking, which is essential to normal coagulation, is still under dispute, being variously ascribed to some deficiency in prothrombin, thrombin, thrombokinase, fibrinogen, or the blood platelets. Gelston[9] favours the view that it is due to lack of prothrombin. Pearce[10] discussing this question, remarks that "whatever the cause, the results of treatment show that the introduction of whole adult blood will in all cases materially inhibit, and in nearly all cases control, the bleeding, causing a coincident return to normal of the coagulation and bleeding times."

Symptoms.

The predominant feature is hæmorrhage, which may be copious and alarming and thus ensure prompt attention, or slight in amount, when it may be permitted to continue for days before advice is sought. Anorexia of varying degree is usual, and has been observed in some cases before the onset of bleeding. The temperature is variable; it may remain normal, but is more frequently subnormal, though on occasion, especially at the onset, slight fever is present. Pallor, cyanosis, coldness of the extremities, weakness or collapse may follow, the degree of collapse being proportionate to the amount of blood-loss.

The diagnosis is usually obvious. Difficulty may arise when internal bleeding alone occurs, but this is extremely rare. In cases of hæmatemesis or melæna due to swallowed blood, the bleeding is invariably small in amount and there are no signs of constitutional disturbance.

The course of the disease is limited by recovery or death; in fatal cases death usually occurs within 1 to 3 days of the onset.

Analysis of Case Histories of Present Series.

24 cases of "hæmorrhagica neonatorum" were admitted to the Royal Hospital for Sick Children, Glasgow, during the period August, 1915, to November, 1926, inclusive. Examination of the histories indicates that the sex incidence is practically equal, 54 per cent. being males and 46 per cent. females. This is in agreement with the findings of most writers.

Only a few instances are recorded in the literature of any familial tendency to the disease. Gelston quotes a case of Reichard's, a ninth child, whose brother died at the age of 4 days of gastro-intestinal hæmorrhage. There is a similar case in the present series.

Case 1. M., boy, aged two days. The mother, aged 40, had had 4 previous pregnancies: (1) girl, aged 6 years, alive and well; (2) boy, melæna at 2 days, responded to treatment, but died, *æt.* 10 weeks, of debility; (3) abortion at 2 months; (4) abortion at 2 months; (5) patient.

The patient was well developed at birth, but pale. Six hours after birth hæmatemesis and melæna occurred. 20 c.cm. of human blood were injected subcutaneously, but melæna continued.

26.4.26. Admitted to Hospital. 10 c.cm. of human blood injected subcutaneously.

27.4.26 Child very pale, lips cyanosed, melæna still present. Blood :—Hb., 40% ; Red B.C., 1,760,000 ; White B.C., 5,600.

28.4.26. Bleeding stopped but general condition of child not improved. Blood transfusion performed because of anæmia. 100 c.cm. of an uncle's blood given intravenously.

29.4.26. Hb., 72% ; Red B.C., 4,070,000 ; White B.C., 14,800. No further bleeding occurred. Child's colour was good. Made good recovery.

In no case was a source of sepsis found nor any lesion suggestive of syphilis.

In 18 of the 24 cases under consideration pregnancy and labour were normal, with the birth of full-time, apparently normal, infants. In the 6 remaining cases labour was abnormal, being premature in 3 cases, instrumental in 2 cases, and in the 6th (a breech presentation) trauma must be admitted as a possible factor, though delivery was spontaneous.

The site of bleeding is various, and for comparison the relative frequency of different sources, as detected later by clinical and post-mortem observation in the present series and in that of Townsend, are placed in parallel columns. (Table II.)

TABLE II.

Sites of Hæmorrhage.

Site of Hæmorrhage.	Present Series. (24 Cases)	Townsend's Series. (50 Cases)
Intestine	17	20
Stomach	15	14
Mouth	5	14
Nose	4	12
Umbilicus	7	18
Skin	11	21
Meninges	1	4
Brain	3	1
Cephalhæmatoma	2	2
Abdomen	2	1
Pleura	1	1
Lungs	5	1
Thymus	1	1
Pericardium	2	0
Kidneys	1	0

Most authorities agree that the average time of onset of the bleeding is from the 2nd to the 4th day after birth. In Fall's[11] series of 14 cases it ranged from the 1st to the 14th day. In Townsend's series of 50 cases, in all but three, the onset was during the first week of life, the exceptions being one on the 8th, 9th and 14th days respectively. The details regarding time of onset in the present series are given in Table III. compared with the findings of Townsend.

TABLE III.

TIME OF ONSET OF BLEEDING.

Time of Onset.	Present Series.	Townsend's Series.
At birth	2	0
During 1st day	6	2
„ 2nd day	11	13
„ 3rd day	2	16
„ 4th day	0	8
„ 5th day	6	0
„ 8th day	0	1
„ 9th day	0	1
„ 14th day	1	1
„ 21st day	1	0

In two instances in the present series an unusually delayed onset of bleeding was observed. It is remarkable that on both occasions it was in the case of children born 8 and 6 weeks prematurely, which may in some way have been responsible for the delay in its appearance. Details of these cases are :—

CASE 2. M. D., male child, aged 14 days. The mother, aged 41, had had 15 previous pregnancies of which seven terminated in stillbirths and one in a miscarriage. In the case of the patient the pregnancy was normal, labour 8 weeks premature, but delivery spontaneous. The infant was said to be jaundiced at birth. There was no history of rash, snuffles, conjunctivitis or convulsions. The child was breast fed, throve, and was apparently healthy. The cord separated on the 9th day, and the umbilicus seemed quite normal until the 14th day, when constant oozing of blood was noted therefrom. The child came under observation that night (aged 14 days). On examination he was small and jaundiced, with oozing of venous blood from the umbilicus. Nothing further abnormal was detected with the exception of a palpable spleen. Local pressure was applied to the umbilicus by gauze pads steeped in adrenalin but 9 hours later the child died.

An autopsy revealed marked jaundice of the skin and liver (the bile ducts, however, were patent). The spleen was larger and softer than normal. Several large hæmorrhages over the base of the brain and also meningeal hæmorrhages were seen. No gross lesion was found in the other organs.

CASE 3. M., female child, six weeks premature, aged 21 days. The mother had had three previous pregnancies and the children are alive and well. While pregnant with patient the mother had during the last 5 weeks recurrent uterine hæmorrhages. The infant, 6 weeks premature, seemed healthy at birth, and moved and cried readily. She was breast fed and sucked well for 3 days and was then artificially fed with cow's milk. Increasing anorexia was noted after the 3rd day. On the 21st day hæmatemesis occurred and the child was brought to hospital in a moribund condition, the tissues were depleted, the eyelids discoloured and the pulse feeble and running. Blood : Hb., 61% ; Red B.C., 2,780,000 ; White B.C., 3,200. On admission 10 c.cm. maternal blood were injected subcutaneously, but no improvement followed, and the child died soon after. The post-mortem examination revealed distention of the pericardial sac with fresh blood, also hæmorrhages in both lungs and blood in the pleural sacs. The stomach contained altered blood, and the brain showed numerous petechial hæmorrhages on its surface. The C.S.F. was blood-stained. Hæmorrhages were also found in the thymus and in the peritoneal sac.

Fatal Cases. In the present series of 24 cases 8 infants died and autopsies were held on 7 of these. The situation of the bleeding was as follows :—

Abdominal Cavity, 1 ; Stomach 1 ; Intestines 3 ; Thymus 1 ; Lungs 5; Pleura 1 ; Pericardium 2 ; Kidneys 1 ; Bladder 1 ; Meninges 1 ; Brain 3.

It is interesting to note that in three cases intracranial hæmorrhage occurred, and that in all birth was premature. Two of these cases are reported in detail above (Cases 2 and 3). The history of the other case is as follows :—

Case 4. A male child, aged 5 days. The mother was healthy during pregnancy but the labour was difficult, instruments being used. The child was 1 month premature, and breathed well at birth but did not cry for 15 minutes after birth. The child was spoon fed and did fairly well for 2 days and then bleeding from the mouth and nose was noted, continuing for 2 days. Child came under observation on the 5th day when slight bleeding from the mouth was observed, also a large hæmatoma over the right parietal bone. The child was small and poorly nourished, with generalised cyanosis, and also sclerema of the body. There was generalised spasticity affecting principally the legs. The child died 3½ hours after admission. A post-mortem examination showed multiple hæmorrhages into the lungs, and congestion of the liver, spleen and kidneys, but no gross lesion in the peritoneum or bowel. There was a large cephalhæmatoma on the right side of the skull posteriorly, and around this were numerous hæmorrhages into the scalp tissues. A large hæmorrhage was found over the vertex of the brain chiefly on the right side where it extended some distance into the cortical layers.

Warwick[12] in a series of 200 necropsies on the newly born, including 41 cases of hæmorrhagic disease showing multiple hæmorrhages, found cerebral hæmorrhages in 20 cases. Rodda had already shown that " hæmorrhagica neonatorum " may be an important factor in the causation of intra-cranial hæmorrhage. He differentiates between hæmorrhage due to trauma and that due to hæmorrhagic disease by the fact that in the former the coagulation and bleeding times fall within normal limits. Foote[13] also expresses the opinion that intracranial hæmorrhage may be a manifestation of " hæmorrhagica neonatorum." He advises early lumbar puncture and the injection of substances to increase blood coagulability in all cases of suspected intracranial hæmorrhage in the newly born. Sharpe[14] on the other hand, maintains that "hæmorrhagica neonatorum " is a rare cause of intracranial hæmorrhage in the new born, and in this connection the predisposition of the premature to cerebral hæmorrhage must be borne in mind.

Treatment.

The first notable advance in the treatment of this disease was in 1910 when Welch[15] advocated the use of injections of normal horse serum. The more recent adoption of whole human blood therapy, either by subcutaneous, intramuscular or intravenous injections, has further considerably decreased the mortality (Table IV.) Thursfield[16] in 1913 remarked that the condition is serious and generally fatal. Holt, however, in 1922, stated that " no case should be looked upon as hopeless, for recovery has repeatedly taken place after transfusion of blood when the infant was moribund."

TABLE IV.

MORTALITY.

Author.	No. of Cases.	Treated by Transfusion.	Number Died.	Mortality, %
Townsend (1894)	50	None	31	62·0
Robertson, Brown and Simpson (1921)	43	All	1	2·3
Fall (1923)	14	All	0	0·0
Present Series (1926)	24	2	8	33·3

The treatment adopted in the present series varied in different cases as follows :—

TABLE V.

RESULTS IN PRESENT SERIES.

Method of Treatment.	No. of Cases.	Recovered.	Died.
Subcutanecus injections of normal horse serum ..	8	5	3
Subcutaneous injections of human blood (alone) ..	10	7	3
Subcutaneous injections of human blood and horse serum	2	2	0
No treatment, death immediately after admission ..	2	0	2
Subcutaneous injections and intravenous transfusions of human blood	2	2	0

Details of one of the cases treated by transfusion has already been given (Case 3). The details of the second are as follows :—

CASE 5. Male, aged 3 days. The mother had had ten previous pregnancies. All the children are living and well. Labour in this case was prolonged, but non-instrumental. The patient was apparently normal at birth, but 2 days later commenced to bleed from the cord. This was ligatured : the bleeding was controlled temporarily, but recurred.

29/9/26. Admitted to Hospital, aged 3 days. Physical examination showed the child to be in good condition, but there was considerable oozing of venous blood from the cord to which pressure was applied with gauze soaked in adrenalin, and at 5 p.m., 20 c.cm. of an uncle's blood were injected subcutaneously. Copious oozing from the cord continued : 6 hours later (11 p.m.) blood transfusion was performed, 80 c.cm. of Dr. S. G's. blood being given.

3/10/26. No further bleeding occurred after transfusion.

Having regard to the short course and the urgency of the symptoms in "hæmorrhagica neonatorum," it is now generally accepted that the ideal method of treatment is by blood transfusion. It is acknowledged, however, that in the

less severe examples subcutaneous or intramuscular injections of whole human blood, or failing this, of normal horse serum, may control the bleeding; but it must be remembered that such injections do not relieve any consequent anæmia. In all severe cases, and especially where anæmia is profound, blood transfusion is indicated, and in fact may be essential to recovery. In the opinion of such observers as Cherry and Langrock[18], de Biasi[19], Falls and Pearce, either parent, but preferably the mother, is the most suitable donor and obviates preliminary compatibility tests. On the other hand, Jones[20], Happ[21] and Learmouth[22], consider that preliminary cross agglutination tests are necessary in all cases because of the fact that occasionally iso-agglutinins and iso-hæmolysins are present in the blood of the new born infant. Doan[23] in a recent comprehensive review of the problem also advises such preliminary cross testing of bloods as being the safer course in the light of present day knowledge. On account of its comparative simplicity the transfusion of citrated blood, the so-called indirect method, is usually performed nowadays. The route selected depends on the choice of the operator and may be the internal saphenous vein at the ankle, the external jugular vein, the longitudinal sinus, etc. The amount of blood transfused is generally estimated at 30 c.cm. per kilogrm. of body weight of the infant.

The results of treatment by transfusion are distinctly encouraging. In Fall's series of 14 cases, many of which had had previous unsuccessful treatment by injections of whole blood or horse serum, recovery followed in every case after transfusion. In all of these cases the mother was used as donor, preliminary cross agglutination tests were not performed, and no reaction occurred. Robertson, Brown and Simpson, in their 43 cases similarly treated, had only one death; these writers carried out cross agglutination tests before selecting a donor. In the present series only 2 cases were treated by transfusion and both recovered; both children had been previously treated by subcutaneous injections of human blood without apparent benefit.

In view of the fact that transfusion gives the best result in these cases, it would be advisable, in the event of either parent proving unavailable or unsuitable as donor, to have on hand suitable donors whose presence could be insured with a minimum loss of time. Properly controlled, a band of voluntary donors as suggested by the Red Cross Society would undoubtedly perform valuable service in such an emergency. The condition is one of urgency and necessitates prompt and efficient treatment, as any delay renders the chances of recovery more remote.

Conclusions.

1. It would appear that the sex incidence of the children affected is practically equal.

2. Infants in the first week of life, especially within the first four days, most frequently exhibit the condition.

3. The question of natal trauma as a factor in the present series only arises in three cases (two instrumental deliveries and one breech presentation).

4. It is suggested that the determination of the coagulation and bleeding times would assist in the diagnosis between hæmorrhage due to trauma and the true hæmorrhagic disease.

5. Examination of the blood is helpful for estimating the gravity of the condition from the amount of blood lost.

6. From the facts and figures available it is apparent that the most efficient and satisfactory treatment is the injection of whole human blood Transfusion is essential in all cases where the constitutional symptoms are severe.

REFERENCES.

1. Holt, L. E., *Diseases of Infancy and Childhood*, N.Y., 1922, 98.
2. Grandidier, Quoted by Townsend, *Arch. Pediat.*, N.Y., 1894, XI, 559.
3. Capon, N. B., *Lancet*, Lond., 1924, i, 1203.
4. Townsend, *Boston Med. & Surg. J.*, Boston, 1891, CXXV, 218.
5. Hess, A. F., *Arch. Pediat.*, N.Y., 1904, XXI, 598.
6. Abt, I. A., *J. Amer. Med. Ass.*, Chic., 1903, XL, 204.
7. Rodda, F. C., *Amer. J. Dis. Child.*, Chic., 1920, XIX, 268.
8. Gibbs, O. S., *Quart. J. Med.*, Oxf., 1924, XVII, 31.
9. Gelston, C. F., *Amer. J. Dis. Child.*, Chic., 1921, XXII, 351.
10. Pearce, N. O., *Abt's Paediatrics*, Philad., 1923, II, 354.
11. Falls, F. H., *J. Amer. Med. Ass.*, Chic., 1923, LXXX, 678.
12. Warwick, M., *Amer. J. Dis. Child.*, Chic., 1921, XX, 492.
13. Foote, J. A., *Ibid*, 1920, XX, 18.
14. Sharpe, W., *J. Amer. Med. Ass.*, Chic., 1923, LXXXI, 620.
15. Welch, *Amer. J. Med. Sc.*, Philad., 1910, CXXXIX, 800.
16. Garrod, A. E., Batten, F. E., & Thursfield, H., *Dis. of Children*, Lond., 1913, 92.
17. Robertson, B., Brown, A., & Simpson, R., *Northwest Med.*, Toronto, 1921, XX, 233.
18. Cherry, T. H., & Langrock, E. G., *J. Amer. Med. Ass.*, Chic., 1916, LXVI, 216.
19. De Biasi, B., *Ibid.*, 1923, LXXXI, 1776.
20. Jones, B. B., *Amer. J. Dis. Child.*, Chic., 1921, XXII, 586.
21. Happ, W. M., *J. Exp. Med.*, N.Y., 1920, XXXI, 313.
22. Learmonth, J. R., *Glasgow Med. J.*, Glasgow, 1924, CI, 116.
23. Sharpe, W., *J. Amer. Med. Ass.*, Chic., 1923, LXXX, 620.

A STUDY OF TWO TYPES OF VOMITING ASSOCIATED WITH ACETONURIA.

BY

O. C. M. DAVIS, M.D., D.Sc.

Physician to Royal Hospital for Sick Children, Bristol.

Lecturer in Chemistry in University of Bristol.

In the present paper are recorded observations on two main types of vomiting occurring in children, which are accompanied by acetonuria. The first part of the paper deals with some theoretical considerations and the second part with a series of actual cases which have come under my notice. The study of these types of vomiting is of interest not only from a clinical point of view, but also from a biochemical standpoint, it being possible, as described later, to follow certain metabolic processes occurring during the attacks, by means of simple analyses of urine.

I. Theoretical Considerations.

It will not be out of place at the outset to refer to the difference between "acidosis" and "ketosis" and their relation to alkali reserve. Acidosis was at one time referred to as a condition in which acetone bodies are present in the urine, but this state is more correctly called ketosis. From a clinical standpoint acidosis may be looked upon as a condition in which there is an abnormal tendency for acid products of metabolism to accumulate in the blood and tissues.

The two conditions may occur side by side, but acidosis is frequently preceded by ketosis, and if in such cases the alkali reserve is maintained by suitable treatment, including the administration of bases, this tendency for acids to accumulate may be rapidly checked.

The importance of recognising conditions where acid formation is increased cannot be over-estimated, for comparatively small variations in the *p*H of blood are incompatible with life. This fact is well illustrated by the many observations recorded in Michælis[1] where the value of *p*H for blood in numerous diseases isgi ven. In only one case[2] does this depart to any great extent from the value in health, 7·3—7·5, namely, in a case of diabetic coma where just before death the values for two determinations were 7·11 and 7·13. De Wesselow[2] quotes a case where the value was 6·98 in a patient with diabetic coma who subsequently recovered under insulin treatment. The *p*H of urine on the other hand may vary within much wider limits, and without serious consequences, the kidneys helping to remove accumulating acids from the blood and tissues.

Group 1. *Cyclic or Recurrent Vomiting.*

The main features of this disease have been so ably dealt with by numerous writers that it is unnecessary to refer to them in great detail, but a few references may be given.

J. P. C. Griffith[3] considers that the condition is a toxic neurosis occurring in especially predisposed children, and due to disordered metabolic processes with inability to assimilate fat.

Ewing[4] considered it to be due to a poisoning from the intestinal tract, with resulting imperfect oxidation of fats.

Richardiere[5] states that the occasional occurrence of icterus has led some to believe that the liver is at fault.

H. C. Cameron[6] in a recent paper, referring to the characteristics of the child subject to cyclical vomiting, writes: "such children often, if not invariably, have certain temperamental and certain physical peculiarities which render their immediate recognition not at all difficult."

H. Membrat[7] agrees with Marfan in considering the cyclic vomiting of the Americans and the vomiting with acetonæmia as forming a single morbid entity, and in the course of his paper refers to the influence of parentage on this disease, the parents having frequently sedentary occupations.

I am strongly inclined to the view that true cyclic vomiting is a clinical entity, associated with a nervous diathesis, and not merely a form of vomiting accompanied by acetonuria.

An outstanding symptom of this condition is the recurrence of attacks of severe vomiting at fairly regular intervals, the exciting cause being some alimentary disturbance, over-exertion, or mental strain. In a severe attack the patient becomes comatose, and in even the milder attacks some drowsiness is usually present. This is probably, at least in part, due to the presence of acetone in the blood, the chemical constitution of this body giving it hypnotic properties.

It has been suggested[8] that adsorption phenomena play an important part in the action of such substances as this, and also that alimentary toxins are adsorbed by the cerebral tissues. The general severity of the symptoms may also be due to some extent to absorption by the bowel of small quantities of undigested protein which act as allergic substances and produce shock. In support of this view is the fact that joint pains occur as in serum disease.

An important question arises as to how many attacks of sickness should warrant the diagnosis of cyclic vomiting. I have personally seen few children who have had a sufficient number of attacks to justify such a diagnosis, but have seen a considerable number of cases which I have placed in the next group.

Group 2. *Severe Acetonuric Vomiting due to Digestive Disturbances.*

Under this heading I refer to an acute alimentary disturbance associated with acetonuria, but in which no neurotic basis is evident.

Some authorities do not definitely distinguish between this condition and true recurrent vomiting, but John Thomson[9] draws attention to "physiological acetonæmia" which has some points in common with the type of disease here described. When we consider that during early life the digestive mechanisms have not reached their maximum degree of efficiency, it is not surprising that at this time disorders of metabolism are quite common.

In the practice of pædiatrics one of the most difficult problems which arise is that of advising suitable food for infants and young children, and the failure of mothers to grasp the principle of physiologically balanced feeding is frequently the underlying cause of digestive disturbances during childhood.

The main symptoms exhibited by children suffering from this type of vomiting are very similar to those described under cyclic vomiting. There is a considerable variation in the degree of severity of an attack, and in some cases the acuteness of the symptoms causes great alarm to parents.

The most important point in differential diagnosis is that the number of attacks is usually limited to one or two, which does not justify the term "cyclic" or "recurrent."

I consider that cases belonging to this class are not uncommon and are possibly diagnosed as cyclic vomiting or acidosis. They are often referred to as bilious attacks by the parents.

II. Clinical and Chemical Investigation of Cases.

A very large number of researches has been carried out on the value of blood analysis in diseases of metabolism, and many valuable results have been obtained: in pædiatric practice, however, the main objects of the clinician should be to hasten the recovery of sick children and prevent future recurrences of disease, and it is not justifiable to take frequent specimens of blood as a routine practice when the course of a disease can be followed by simple methods.

In the investigations here described a method of urine analysis has been adopted which was referred to in a short paper[10] read before the Children's Section of the Royal Society of Medicine in 1923 and has been discussed in greater detail[11,12] in two subsequent papers.

The ratio Ra referred to actually denotes the relationship between free and ammonia-combined acid in the urine, and is obtained as follows:—

25 c.cm. of urine are titrated with decinormal sodium hydroxide solution, using as indicator phenolphthalein; this gives the free acid value. Then to the same solution neutral formaldehyde solution is added (Folin's method) to liberate ammonia-combined acid which is then titrated with the same alkaline solution.

Ra is obtained by dividing the second titration by the first. The ratio is not reliable when determined during the administration of alkalis.

Acetone is tested for by adding to the urine a few drops of freshly-prepared solution of sodium nitro-prusside, acidifying with glacial acetic acid, and floating ·880 ammonia solution on the top of the mixture. A magenta ring forms at junction of the two liquids in presence of acetone.

The above titrations to obtain the ratio Ra are extremely simple, and can be carried out rapidly after little practice. They enable the physician to correlate the clinical and the bio-chemical events during the course of an attack.

It will be commonly found that during early stages of the "attacks" described later, acetone may be detected in the urine before the magnitude of Ra is increased, pointing to the probability of a good alkali reserve (see Case 1).

Case Records.

Group 1. *Cyclic Vomiting.*

Case 1. I have been able to obtain early morning specimens of urine from a little girl who undoubtedly suffered for several years from true cyclic or recurrent vomiting.

These attacks were originally considered to be " bilious attacks " until more careful consideration was given to the case and numerous analyses of her urine were made. The patient possesses a very nervous disposition, and worries over small matters; the attacks were associated with faults in diet, and physical or mental strain, one such attack being initiated by a prolonged railway journey. During each attack the patient was repeatedly and violently sick, the temperature being raised and pulse accelerated. These symptoms were associated with great prostration and various degrees of lethargy approaching coma; there were severe pains in the muscles and joints, and occasionally abdominal discomfort. One attack at the age of 8 years lasted 6 days, and a similar one at 11 years lasted for the same time. It is worthy of note than the child recently had a severe attack of a similar nature although now 13 years of age.

TABLE I.

Case I. Urine Analysis: Early morning specimens.

	Titration I.	Titration II.	Ra	Acetone Bodies.
In normal health.	7·3	7·9	1·08	Absent.
	16·0	16·0	1·00	,,
	15·1	16·0	1·05	,,
	14·0	15·0	1·07	,,
	11·5	14·2	1·23	,,
	14·8	16·8	1·13	,,
	16·7	14·6	0·87	,,
	9·0	10·0	1·11	,,
During attack.	9·5	11·9	1·25	Present
	14·9	31·6	2·12	,,
	13·0	23·2	1·78	Absent.
	12·0	16·5	1·37	,,
	8·7	13·0	1·49	,,
During another attack.	9·9	34·0	3·43	Present.
	4·8	21·5	4·47	,,
	6·1	25·0	4·09	,,
	10·2	16·0	1·56	Absent.
	12·2	16·5	1·35	,,
	11·2	15·1	1·34	,,

Case 2. This was a little girl, an only child, aged $5\frac{3}{4}$ years. There was a history of constipation, associated with occasional severe attacks of vomiting; a recent one being accompanied by albuminuria. When first seen by me she was very drowsy. T. 101°, and had vomited at half-hourly intervals. The bowels were constipated, and the urine contained albumin (·07 Esbach) and acetone bodies.

TABLE II.

Case 2. Urine Analysis: Morning specimen.

Titration I.	Titration II.	Ra	Acetone Bodies.
11·5	47·0	4·13	Present.

The patient was discharged fit after six days treatment with alkalis and laxatives. I have been informed by the child's doctor that she has had a number of similar attacks since, and at the time of writing she is under my care in hospital for the same trouble.

Case 3. The history of another case of true cyclic vomiting seems worth recording as the attacks have extended over a period of ten years.

The patient, a girl, aged 13 years, was seen by me recently after an operation for tendon transplantation; she had been vomiting frequently for four days after the operation and the urine contained large amounts of acetone bodies. Sodium bicarbonate and calomel soon relieved the symptoms, but as the administration of alkalis renders the value of Ra unsatisfactory this ratio was not followed.

From the hospital records I found that she had a severe attack of a similar nature when 7 years old after tonsillectomy and the following year an attack simulating acute intestinal obstruction. Her mother also described numerous other attacks of acute vomiting.

Group II. Severe Acetonuric Vomiting or Toxæmic Vomiting of Childhood with Acetonuria.

As previously pointed out cases included in this group are relatively common. I have been able to follow a number of them, especially with reference to the variations which occur in the urine normally and during an attack. I propose to refer to several of these cases in some detail.

Case 4. This patient is the younger sister of Case 1, but does not possess the same type of nervous temperament, and appears to be quite a normal child. She had a brief attack of acetonuric vomiting at 2 years of age and a much more severe one at 5 years. The latter attack started on the day following faulty feeding.

She was greatly distressed, very sleepy, pulse 140, respirations 36, temperature 102°, and complained of pains in the neck and joints. The urine on the first day of attack contained much acetone. The symptoms rapidly disappeared after administration of laxatives.

TABLE III.

Case 4. Urine Analysis: Early morning specimens.

	Titration I.	Titration II.	Ra	Acetone Bodies.
In normal health.	3·8	4·7	1·23	Absent.
	23·0	20·0	0·87	„
	16·1	16·3	1·01	„
	4·4	5·4	1·20	„
	5·0	6·0	1·20	„
	22·7	21·8	0·96	„
During attack and recovery.	31·30	37·5	1·19	Present.
	14·50	30·5	2·10	Absent.
	14·0	24·5	1·75	„
	2·7	5·1	1·88	„
	4·0	8·0	2·0	„
	11·5	14·1	1·21	„

The alkali reserve was doubtless diminished during the attack, but rapidly recovered on normal diet without administration of bases. The child has had no further similar attacks, and is now seven years old.

Case 5. A girl aged 9¾ years. This case is of special interest since, although the symptoms on admission were identical with those observed in a severe case of cyclic vomiting, there was no history of recurrent attacks.

When admitted to hospital the child looked extremely ill and collapsed. The respirations were those of "air hunger," the eyes were half closed, and the patient in a comatose condition.

When roused and questioned she complained of pains in the belly and joints. The tongue, tonsils, and uvula were covered with a dark brown deposit, the temperature raised and pulse accelerated.

The child was given a soap enema and then sodium bicarbonate, gr. 20, every four hours, and was very much better next day. A specimen of urine passed on admission was loaded with acetone, but as is frequently the case at the onset of such attacks gave no indication of acidosis (RA=0·91). Owing, however, to the serious condition of the child it was deemed wise to administer alkalis immediately, which prevented RA from being satisfactorily followed, as the urine soon became alkaline to phenolphthalein. The urine also contained a trace of albumin on admission, but this rapidly disappeared, as did the acetone bodies. She has had no further attack.

CASE 6. Patient, a boy aged four years, who had vomited a number of times before admission; on the day he entered hospital his urine contained acetone bodies. He was given no drugs but kept on low diet, and was discharged fit after seven days.

TABLE IV.

CASE 6. URINE ANALYSIS: Early morning specimens.

	Titration I.	Titration II.	RA	Acetone Bodies.
During attack and recovery.	6·3	15·7	2·47	Present.
	10·0	42·5	4·25	,,
	7·0	18·0	2·57	Absent.
	10·0	15·5	1·55	,,

His mother informed me eight months later that he was quite well, and that he had suffered from no similar illness either before or after the one described here.

CASE 7. This case is very similar to the previous one. The patient, a boy aged 5½ years, had vomited five times in the twelve hours before admission, and was constipated.

On admission his temperature was 101°, and his pulse rate 142. No further vomiting occurred; calomel was administered and early morning urine examined for three days. The results distinctly indicating acidosis the boy was given sodium bicarbonate for six days, and was discharged quite fit two days later. There was no history of any similar attack.

TABLE V.

CASE 7. URINE ANALYSIS: Early morning specimens.

	Titration I.	Titration II.	RA	Acetone Bodies.
First three mornings in hospital.	13·0	31·0	2·38	Present.
	11·0	39·0	3·54	,,
	4·0	28·0	7·0	,,
Morning of discharge	15·5	20·0	1·29	Absent.

CASE 8. The patient, a boy aged three years, had an attack of frequent vomiting, and on admission to hospital his urine contained acetone bodies, and his temperature was 101°.

He was placed on low diet and treated with calomel. As the ratio RA was not diminished by this treatment he was given sodium bicarbonate and rapidly improved.

I was unable to elicit any history of other attacks, and ten months later his father informed me that he was in good health.

TABLE VI.

Case 8. Urine Analysis.

	Titration I.	Titration II.	Ra	Acetone Bodies.
Before treatment with alkalis.	11·0	17·5	1·59	Present.
	11·5	22·5	1·95	,,
	6·5	15·5	2·38	,,

Case 9. A girl, aged 8 years, had two attacks of severe vomiting within two months. On both occasions the sickness was associated with drowsiness, raised temperature, accelerated pulse and acetonuria.

On the first occasion she was treated with sodium bicarbonate and calomel, and on the second occasion with calomel and glucose without alkalis. The analyses of several early morning specimens of urine during attack and recovery serve to demonstrate that the ratio Ra is not reliable during administration of alkalis.

TABLE VII.

Case 9. Urine Analysis: Early morning specimens.

	Titration I.	Titration II.	Ra	Acetone Bodies.
Under alkaline treatment,	17·5	26·5	1·51	Present.
	9·0	24·5	2·72	,,
	2·5	6·5	2·60	Absent.
Under glucose treatment.	9·0	32·0	3·55	Present.
	12·0	26·0	2·17	,,
	16·5	31·0	1·87	Absent.
	11·6	17·0	1·46	,,

On both occasions recovery was rapid, and nine months later the child was in good health, and had not suffered from a similar illness in the interval.

Case 10. A little girl aged 15 months, who had vomited eight times in twenty-four hours. On examination the child was very irritable, temperature 101°, pulse 160. She had been given an excess of milk and eggs for some time. An examination of the urine gave following results :—

TABLE VIII.

Case 10. Urine Analysis.

Titration I.	Titration II.	Ra	Acetone Bodies.
13·5	49·0	3·62	Present.

Calomel and sodium bicarbonate were administered at once and the patient was virtually normal next day. The child had a similar but less severe attack nine months later, but her doctor informs me that since this she has had no more attacks, and she is now three and a half years of age.

Case 11. In this case the patient was a little girl who suddenly became ill after over-indulgence in rich diet. She was violently sick, temperature raised and pulse rate much accelerated, and finally lapsed into a lethargic condition. The urine was mixed with vomit and could therefore not be examined quantitatively, but gave well marked reactions for acetone.

Administration of calomel restored her to an almost normal condition next day, despite the severity of the attack. She had no similar attack previously, and three years later her doctor informed me that she had experienced no further trouble of the kind.

It is well to remember that the early stages of tuberculous meningitis may simulate acetonuric vomiting. Such a case was referred to me, and a urine examination gave :

TABLE IX.

TUBERCULOUS MENINGITIS. URINE ANALYSES.

Titration I.	Titration II.	Ra	Acetone Bodies.
10·0	30·0	3·0	Present.

Shortly afterwards typical signs of tuberculous meningitis were present, and the patient died within a week.

It would be unprofitable to describe in detail further cases belonging to this group, but they frequently come under my observation, and I have a number of records of patients in which only one or two attacks were observed but which were very severe and caused much anxiety to the parents. The symptoms observed in such an attack are clinically indistinguishable from those noticed in one of the periodic attacks occurring in true cyclic vomiting.

It is worthy of note that there is nearly always a history of marked dietetic indiscretion preceding the attacks. The treatment is by means of low diet, aperients, and rest, with the addition of alkalis if indicated by severity of the case or by urine analysis.

SUMMARY.

Two types of acetonuric vomiting in children have been described, and special reference has been made to the urinary findings in each type.

It has also been shown that the course of the disease can be followed by means of simple urine analysis. In both types a variable degree of acidosis and ketosis is observed.

The ease with which these conditions develop in children is responsible for some of the symptoms described, and points to the necessity for early administration of bases in many cases.

I have ventured to draw a very definite line between true cyclic vomiting and severe acetonuric vomiting, as this distinction appears to be justified by careful investigation of the clinical histories.

I wish to thank the Colston Research Committee for a grant towards expenses of this investigation.

REFERENCES.

1. Michaelis, L., *Die Wasserstoffionen konzentration*, Berlin, 1914, 103.
2. De Wesselow, O. L. V., *Chem. of Blood in Clin. Med.*, Lond., 1924, 55.
3. Griffith, J. P. C., *Diseases of Children*. Philad. 1920, 702.
4. Ewing, J., *Studies from Dept. of Pathology*. Cornell Med. Coll. 1908, VIII.
5. Richardiere, H., *Ann. de méd. et de chir. infan.*, Paris, 1905, IX, 150.
6. Cameron, H. C., *Arch. Dis. Childhood*, Lond., 1927, II, 56.
7. Membrat, H., *J. de méd de Bordeaux*, Bord., 1926, III, 102.
8. Davis, O. C. M., *Med. Chir. J.*, Bristol, 1920, XXXVII, 5.
9. Thomson, J., *Clin. Study and Treatment of Sick Children*, Edin., 1921, 453.
10. Davis, O. C. M., *Brit. Med. J.*, Lond., 1923, ii, 21.
11. Davis, O. C. M., and Rixon, F. W., *Clin. J.*, Lond., 1925, LIV, 65, 75.
12. Davis, O. C. M., and Rixon, F. W., *Brit. Med. J.*, Lond., 1927, i, 758.